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- (54) Probes and method to detect human immunodeficiency virus type 1.
- Amplification oligonucleotides and hybridization assay probes are provided which distinguish Human Immunodeficiency Virus type 1 from other viruses found in human blood tissues.

  The probes are nucleotide polymers which hybridize to the nucleic acid region of Human Immunodeficiency Virus type 1 corresponding to bases 763-793 of HIV type 1, (HXB2 isolate GenBank accession number KO3455), or any of the regions corresponding to bases 1271-1301, 1358-1387, 1464-1489, 1501-1540, 1813-1845, 2969-2999, 3125-3161, 4148-4170,4804-4832, 5950-5978, 9496-9523, 510-542 and 624-651.

FP 0 617 132 A2

This invention relates to the design and construction of amplification oligonucleotides and probes to Human Immunodeficiency Virus Type 1 (HIV), which allow detection of the organism in a test sample.

Laboratory diagnosis of Human Immunodeficiency Virus Type 1 in humans is currently performed by demonstration of the presence of viral antigen (p24) or anti-HIV-1 antibodies in serum. Direct detection of viral DNA, however, is a more useful diagnostic tool in some populations, such as infants born to seropositive mothers. Detection of viral DNA is more rapid and less hazardous than culture. Direct hybridization lacks adequate sensitivity in most patients (Shaw et al. Science 226: 1165-1171, 1984). Many references mention oligonucleotides said to have use in detection of Human Immunodeficiency Virus. Most of these references also mention the use of polymerase chain reaction (PCR). These references include the following: Kwok et al., J. Virol. 61: 1690-1694, 1987; Agius et al., J. Virol. Meth., 30: 141-150, 1990; Albert and Fenyo, J. Clin. Microbiol. 28:1560-1564, 1990; Bell and Ratner, AIDS Res. and Human Retroviruses 5:87-95, 1989; Bruisten et al., Vox Sang 61:24-29, 1991; Clarke et al., AIDS 4:1133-1136, 1990; Coutlee et al., Anal. Biochem. 181:96-105, 1989; Dahlen et al., J. Clin. Microbial. 29:798-804, 1991; Dudding et al., Biochem. Biophys. Res. Comm. 167:244-250, 1990; Ferrer-Le-Coeur et al., Thrombosis and Haemostasis 65:478-482, 1991; Goswami et al., AIDS 5:797-803, 1991; Grankvist et al., AIDS 5:575-578, 1991; Guatelli et al., J. Virol. 64:4093-4098, 1990; Hart et al., Lancet 2 (8611):596-599, 1988; Holland et al., Proc. Natl. Acad. Sci. USA, 88:7276-7280, 1991; Keller et al., Anal. Biochem. 177:27-32, 1989; Kumar et al., AIDS Res. and Human Retroviruses 5:345-354, 1989; Linz et al., J. Clin. Chem. Clin. Biochem. 28:5-13, 1990; Mano and Chermann, Res. Virol. 142:95-104, 1991; Mariotti et al., AIDS 4:633-637, 1990; Mariotti et al., <u>Transfusion</u> 30:704-706, 1990; Meyerhans et al., <u>Cell</u> 58:901-910, 1989; Mousset et al., AIDS 4:1225-1230, 1990; Ou et al., Science 239:295-297, 1988; Pang et al., Nature 343:85-89, 1990; Paterlini et al., J. Med. Virol. 30:53-57, 1990; Perrin et al., Blood 76:641-645, 1990; Preston et al., J. Virol. Meth. 33;383-390, 1991; Pritchard and Stefano, Ann. Biol. Clin. 48:492-497, 1990; Rudin et al., Eur. J. Clin. Microbiol. Infect. Dis. 10:146-156, 1991; Shoebridge et al., AIDS 5:221-224, 1991; Stevenson et al., <u>J.</u> Virol, 64;3792-3803, 1990; Truckenmiller et al., Res. Immunol. 140:527-544, 1989; Van de Perre, et al., New Eng. J. Med. 325:593-598, 1991; Varas et al., BioTechniques 11:384-391, 1991; Velpandi et al., J. Virol. 65:4847-4852, 1991; Williams et al., AIDS 4:393-398, 1990; Zachar et al., <u>J. Virol. Meth.</u> 33:391-395, 1991; Zack et al. Cell 61:213-222, 1990; Findlay et al., entitled "Nucleic acid test article and its use to detect a predetermined nucleic acid," PCT/US90/00452; Gingeras et al., entitled "Nucleic acid probe assay methods and compositions," PCT/US87/01966; Brakel and Spadoro, entitled "Amplification capture assay," EPO application number 90124738.7, publication number 0 435 150 A2; Moncany and Montagnier, entitled "Séquences nucleotidiques issues du génome des retrovirus du typ hiv-1, hiv-2 et siv, et leurs applications notamment pour l'amplification des génomes de ces retrovirus et pour le diagnostic in-vitro des infections dues a ces virus," EPO application number 90401520.3, publication number 0 403 333 A2; Urdea, entitled "DNA-dependent RNA polymerase transcripts as reporter molecules for signal amplification in nucleic acid hybridization assays," PCT/US91/00213; Musso et al., entitled "Lanthanide chelate-tagged nucleic acid probes," PCT/US88/03735; Chang, entitled "Cloning and expression of HTLV-III DNA," EPO application number 85307260.1, publication number 0 185 444 A2; and Levenson, entitled "Diagnostic kit and method using a solid phase capture means for detecting nucleic acids," EPO application number 89311862.0, publication number 0 370 694; and Sninsky et al., U.S. Patent No. 5,008,182.

### Summary of the Invention

This invention discloses novel amplification oligonucleotides and detection probes for the detection of Human Immunodeficiency Virus Type 1. The probes are capable of distinguishing between the Human Immunodeficiency Virus type 1 and its known closest phylogenetic neighbors. The amplification oligonucleotides and probes may be used in an assay for the detection and/or quantitation of Human Immunodeficiency Virus nucleic acid.

It is known that a nucleic acid sequence able to hybridize to a nucleic acid sequence sought to be detected ("target sequence") can serve as a probe for the target sequence. The probe may be labelled with a detectable moiety such as a radioisotope, antigen or chemiluminescent moiety to facilitate detection of the target sequence. A background description of the use of nucleic acid hybridization as a procedure for the detection of particular nucleic.acid sequences is provided in Kohne, U.S. Patent No. 4,851,330, and Hogan et al., EPO Patent Application No. PCT/US87/03009, entitled "Nucleic Acid Probes for Detection and/or Quantitation of Non-Viral Organisms."

It is also known that hybridization may occur between complementary nucleic acid strands including; DNA/DNA, DNA/RNA, and RNA/RNA. Two single strands of deoxyribo- ("DNA") or ribo- ("RNA") nucleic acid, formed from nucleotides (including the bases adenine (A), cytosine (C), thymidine (T), guanine (G), uracil (U), or inosine (I)), may hybridize to form a double-stranded structure in which the two strands are held together

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by hydrogen bonds between pairs of complementary bases. Generally, A is hydrogen bonded to T or U, while G is hydrogen bonded to C. At any point along the hybridized strands, therefore, one may find the classical base pairs AT or AU, TA or UA, GC, or CG. Thus, when a first single strand of nucleic acid contains sufficient contiguous complementary bases to a second, and those two strands are brought together under conditions which will promote their hybridization, double-stranded nucleic acid will result. Under appropriate conditions, DNA/DNA, RNA/DNA, or RNA/RNA hybrids may be formed. The present invention includes the use of probes or primers containing nucleotides differing in the sugar moiety, or otherwise chemically modified, which are able to hydrogen bond along the lines described above.

Thus, in a first aspect, the invention features hybridization assay probes able to distinguish Human Immunodeficiency Virus type 1 from other viruses found in human blood or tissues, and amplification oligonucleotides able to selectively amplify Human Immunodeficiency Virus nucleic acid. Specifically, the probes are nucleotide polymers which hybridize to the nucleic acid region of Human Immunodeficiency Virus type 1 corresponding to bases 763-793 of HIV type 1, (HXB2 isolate GenBank accession number K03455), or any of the regions corresponding to bases 1271-1301, 1358-1387, 1464-1489, 1501-1540, 1813-1845, 2969-2999, 3125-3161, 4148-4170, 4804-4832, 5950-5978, 9496-9523, 510-542, and 624-651; preferably, the oligonucleotide comprises, consists essentially of, or consists of the sequence (reading 5' to 3')

	(SEQ	ID	NO:	1)	GACTAGCGGAGGCTAGAAGGAGAGATGGG
20	(SEQ	ID	NO:	2)	GAAGGCTTTCAGCCCAGAAGTAATACCCATG
	(SEQ	ID	NO:	3)	ATTTGCATGCTGCTTGATGTCCCCCCACT
	(SEQ	ID	NO:	4)	CTTCCCCTTGGTTCTCTCATCTGGCC
25	(SEQ	ID	NO:	5)	GTCATCCATCCTATTTGTTCCTGAAGGGTACTAGTAG
	(SEQ	ID	NO:	6)	CTCCCTGACATGCTGTCATCATTTCTTCTAGTG
	(SEQ	ID	NO:	7)	GTGGAAGCACATTGTACTGATATCTAATCCC
	(SEQ	ID	NO:	8)	GCTCCTCTATTTTGTTCTATGCTGCCCTATTTCTAA
30	(SEQ	ID	NO:	9)	CCTTTGTGTGCTGGTACCCATGC
	(SEQ	ID	NO:	10)	CTACTATTCTTTCCCCTGCACTGTACCCC
	(SEQ	ID	NO:	11)	AAAGCCTTAGGCATCTCCTATGGCAGGAA
35	(SEQ	ID	NO:	12)	GCAGCTGCTTATATGCAGGATCTGAGGG
	(SEQ	ID	NO:	13)	CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG
	(SEQ	ID	No:	14)	ATCTCTAGCAGTGGCGCCCGAACAGGGA

or RNA equivalents thereto (SEQ. ID. Nos. 67-80), or oligonucleotides complementary thereto (SEQ. ID. Nos. 53-66), or RNA equivalents to the oligonucleotides complementary thereto (SEQ. ID. Nos. 81-94).

The oligonucleotides are used with or without a helper probe as described below. The use of helper probes (<u>e.g.</u>, SEQ. ID. Nos. 15-18) and complementary oligonucleotides to the helper probes (<u>e.g.</u>, SEQ. ID. Nos. 95-98) and RNA equivalents thereto (e.g., SEQ. ID. Nos. 132-140) enhances nucleic acid hybridization.

By "consists essentially of" is meant that the probe is provided as a purified nucleic acid which under stringent hybridizing conditions hybridizes with the target sequence and not with other related target sequences present in either other virus nucleic acids or human nucleic acids. Such a probe may be linked to other nucleic acids which do not affect such hybridization. Generally, it is preferred that the probe is between 15 to 100 (most preferably between 20 and 50) bases in size. It may, however, be provided in a vector.

In a related aspect, the invention features the formation of nucleic acid hybrids formed by the hybridization of the probes of this invention with target nucleic acid under stringent hybridization conditions. Stringent hybridization conditions involve the use 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C. The hybrids are useful because they allow the specific detection of viral nucleic acid.

In another related aspect, the invention features amplification oligonucleotides useful for specific detection of Human Immunodeficiency Virus type 1 in an amplification assay. The amplification oligonucleotides are complementary to conserved regions of HIV genomic nucleic acid and are nucleotide polymers able to hybridize to regions of the nucleic acid of HIV corresponding to HIV-1 HXB2R bases 682-705, 800-822, 1307-1337, 1306-1330, 1315-1340, 1395-1425, 1510-1535, 1549-1572, 1743-1771, 1972-1989, 2868-2889, 3008-

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3042, 3092-3124, 3209-3235, 4052-4079, 4176-4209, 4169-4206, 4394-4428, 4756-4778, 4835-4857, 4952-4969, 5834-5860, 5979-5999, 9431-9457, 9529-9555, 449-473, 550-577, 578-601, 579-600, 624-646, and 680-703.

Specifically, such amplification oligonucleotides consist, comprise, or consist essentially of those selected from (reading 5' to 3'):

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(X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),
     (X)CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),
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     (X)GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),
     (X)GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),
     (X) CAGAAGGAGCCACCCCACAAGATTTA (SEQ. ID. NO. 23),
     (X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),
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     (X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),
     (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26),
     (X) CCATCCTATTTGTTCCTGAAGGGTAC (SEQ. ID. NO. 27),
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     (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),
     (X) GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29),
     (X) TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),
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     (X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),
     (X)GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),
     (X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33),
     (X)ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),
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     (X)GCATTAGGAATCATTCAAGCACCAG (SEQ. ID. NO. 35),
     (X)GCACTGACTAATTTATCTACTTGTTCATTTCCTC (SEQ. ID. NO. 36),
     (X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO.
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     37),
     (X)TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),
     (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),
     (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),
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      (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41),
      (X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),
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      (X) CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),
      (X) CAAGGGACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44),
      (X)GTCTAACCAGAGAGCCCAGTACAGGC (SEQ. ID. NO. 45),
      (X) GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),
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      (X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
      (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
      (X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),
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      (X) GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),
      (X) GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51)
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and the RNA equivalents thereto (SEQ. ID. Nos. 99-131). Where (X) is nothing or a 5' oligonucleotide sequence that is recognized by an enzyme, including but not limited to the promoter sequence for T7, T3, or SP6 RNA polymerase, which enhances initiation or elongation of RNA transcription by an RNA polymerase. One example of X includes the sequence SEQ. ID. NO. 52: 5'-AATTTAATACGACTCACTATAGGGAGA-3'.

These amplification oligonucleotides are used in a nucleic acid amplification assay such as the polymerase chain reaction or an amplification reaction using RNA polymerase, DNA polymerase and RNase H or its equivalent, as described by Kacian and Fultz, <u>supra</u>, and by Sninsky et al. US. Patent No. 5,079,351, both hereby incorporated by reference herein.

The amplification oligonucleotides and probes of this invention offer a rapid, non-subjective method of identification and quantitation of a sample for specific sequences unique to strains of Human Immunodeficiency Virus type 1.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims.

### Description of the Preferred Embodiments

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We have discovered particularly useful DNA probes complementary to particular nucleic acid sequences of Human Immunodeficiency Virus type 1. Furthermore, we have successfully used these probes in a specific assay for the detection of Human Immunodeficiency Virus type 1, distinguishing it from the known and presumably most closely related taxonomic or phylogenetic neighbors found in human blood or tissues.

We have also identified particularly useful amplification oligonucleotides which are complementary to the Human Immunodeficiency Virus type 1 nucleic acid, and have used these oligonucleotides, <u>e.g.</u>, as primers or promoter primer combinations (<u>i.e.</u>, a primer having a promoter sequence attached), to amplify the nucleic acid of Human Immunodeficiency Virus, allowing its direct detection in a sample.

Useful guidelines for designing amplification oligonucleotides and probes with desired characteristics are described herein. The optimal sites for amplifying and probing contain two, and preferably three, conserved regions greater than about 15 bases in length, within about 350 bases, and preferably within 150 bases, of contiguous sequence. The degree of amplification observed with a set of primers or promotor/primers depends on several factors, including the ability of the oligonucleotides to hybridize to their complementary sequences and their ability to be extended enzymatically. Because the extent and specificity of hybridization reactions are affected by a number of factors, manipulation of those factors will determine the exact sensitivity and specificity of a particular oligonucleotide, whether perfectly complementary to its target or not. The importance and effect of various assay conditions are known to those skilled in the art as described in Hogan et al., EPO Patent Application No. PCT/US87/03009, entitled "Nucleic Acid Probes for Detection and/or Quantitation of Non-Viral Organisms"; and Milliman, entitled "Nucleic Acid Probes to Haemophilus influenzae," U.S. Serial No. 07/690,788, filed 4/25/91 assigned to the same assignee as the present application and hereby incorporated by reference herein.

The length of the target nucleic acid sequence and, accordingly, the length of the probe sequence can be important. In some cases, there may be several sequences from a particular region, varying in location and length, which will yield probes with the desired hybridization characteristics. In other cases, one sequence may be significantly better than another which differs merely by a single base. While it is possible for nucleic acids that are not perfectly complementary to hybridize, the longest stretch of perfectly homologous base sequence will normally primarily determine hybrid stability. While oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 10 to 50 bases in length and are sufficiently homologous to the target nucleic acid to hybridize under stringent hybridization conditions. We have found that optimal primers have target-binding regions of 18-38 bases, with a predicted Tm (melting temperature) to target of about 65°C.

Amplification oligonucleotides or probes should be positioned so as to minimize the stability of the oligomer:nontarget (<u>i.e.</u>, nucleic acid with similar sequence to target nucleic acid) nucleic acid hybrid. It is preferred that the amplification oligomers and detection probes are able to distinguish between target and non-target sequences. In designing probes, the differences in these Tm values should be as large as possible (<u>e.g.</u>, at least 2°C and preferably 5°C).

Regions of the nucleic acid which are known to form strong internal structures inhibitory to hybridization are less preferred. Examples of such structures include hairpin loops. Likewise, probes with extensive self-complementarity should be avoided.

The degree of non-specific extension (primer-dimer or non-target copying) can also affect amplification efficiency, therefore primers are selected to have low self- or cross- complementarity, particularly at the 3' ends of the sequence. Long homopolymer tracts and high GC content are avoided to reduce spurious primer

extension. Commercial computer programs are available to aid in this aspect of the design. Available computer programs include MacDNASIS™ 2.0 (Hitachi Software Engineering American Ltd.) and OLIGO• ver. 4.1 (National Bioscience).

Hybridization is the association of two single strands of complementary nucleic acid to form a hydrogen bonded double strand. It is implicit that if one of the two strands is wholly or partially involved in a hybrid that it will be less able to participate in formation of a new hybrid. By designing a probe so that a substantial portion of the sequence of interest is single stranded, the rate and extent of hybridization may be greatly increased. If the target is an integrated genomic sequence then it will naturally occur in a double stranded form, as is the case with the product of the polymerase chain reaction (PCR). These double-stranded targets are naturally inhibitory to hybridization with a probe and require denaturation prior to the hybridization step. Finally, there can be intramolecular and intermolecular hybrids formed within a probe if there is sufficient self complementarity. Such structures can be avoided through careful probe design. Commercial computer programs are available to search for this type of interaction. Available computer programs include MacDNASIS™ 2.0 (Hitachi Software Engineering American Ltd.) and OLIGO\* ver. 4.1 (National Bioscience).

Once synthesized, selected oligonucleotide probes may be labelled by any of several well known methods. 2 J. Sambrook, E.F. Fritsch and T. Maniatis, <u>Molecular Cloning</u> 11 (2d ed. 1989). Useful labels include radio-isotopes as well as non-radioactive reporting groups. We currently prefer to use acridinium esters.

Oligonucleotide/target hybrid melting temperature may be determined by isotopic methods well known to those skilled in the art. It should be noted that the Tm for a given hybrid will vary depending on the hybridization solution being used. Sambrook, et al. supra.

Rate of hybridization may be measured by determining the  $C_ot_{k}$ . The rate at which a probe hybridizes to its target is a measure of the thermal stability of the target secondary structure in the probe region. The standard measurement of hybridization rate is the  $C_ot_{k}$  which is measured as moles of nucleotide per liter times seconds. Thus, it is the concentration of probe times the time at which 50% of maximal hybridization occurs at that concentration. This value is determined by hybridizing various amounts of probe to a constant amount of target for a fixed time. The  $C_ot_{k}$  is found graphically by standard procedure.

The following examples set forth oligonucleotide probes complementary to a unique nucleic acid sequence from a target organism, and their use in a hybridization assay.

### Examples:

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Probes specific for Human Immunodeficiency Virus type 1 were identified by comparison of sequences obtained from the published database GenBank. Sequences ID Nos. 1-12 were characterized and shown to be specific for Human Immunodeficiency Virus type 1. Phylogenetically near neighbors including Human Immunodeficiency Virus type 2, Human T-cell Leukemia Virus type 1 and Human T-Cell Leukemia Virus type 2 were used as comparisons with the sequence of Human Immunodeficiency Virus Type 1.

### Example 1. Probes for HIV

A hybridization protection assay was used to demonstrate the reactivity and specificity of the probes for Human Immunodeficiency Virus type 1. The probes were first synthesized with a non-nucleotide linker, then labelled with a chemiluminescent acridinium ester (AE) as described by Arnold, et al., PCT/US88/03361, entitled "Acridinium Ester Labeling and Purification of Nucleotide Probes," hereby incorporated by reference herein. The acridinium ester attached to an unhybridized probe is susceptible to hydrolysis and rendered non-chemiluminescent under mild alkaline conditions. However, the acridinium ester attached to hybridized probe is relatively resistant to hydrolysis. Thus, it is possible to assay for hybridization of acridinium ester-labelled probe by incubation with an alkaline buffer, followed by detection of chemiluminescence in a luminometer. Results are given in Relative Light Units (RLU); the quantity of photons emitted by the labelled-probe measured by the luminometer.

In the following experiment, DNA prepared from clones containing full or partial sequences of the target viruses was assayed. An example of a method for preparing the DNA from clones is provided by Sambrook et al, <u>supra</u>. The source of DNA for the clones was as follows; Human Immunodeficiency Virus type 1, BH10 (L. Ratner et al., <u>Nature</u> 312:277-284. 1985); Human Immunodeficiency Virus type 2 NIHZ (J.F. Zagury, et al., <u>Proc. Natl. Acad. Sci. USA</u> 85:5941-5945. 1988), Human T-cell leukemia virus type 1 pMT-2, (M. Clarke et al. <u>Nature</u> 305:60-62. 1983); Human T-cell leukemia virus type 2 (K. Shimotohmo et al. <u>Proc. Natl. Acad. Sci. USA</u> 82:3101-3105. 1985); and Human Hepatitis B Virus serotype ADW, obtained from ATCC(# 45020). Target in 50 µl of 10 mM N-2-hydroxyethelpiperazine-N'-2-ethanesulfonic acid (HEPES), 10 mM ethylenediaminetetraacetic acid (EDTA), 1% lithium lauryl sulfate, pH 7.4, was denatured at 95°C for 5 min, cooled on wet ice, and 0.04 pmol of probe in 50 µl of 0.1 M lithium succinate buffer, pH 4.7, 2% (w/v) lithium lauryl sulfate, 1.2 M lithium chloride, 10 mM EDTA and 20 mM ethyleneglycol-bis-(beta-aminoethyl ether) N,N,N',N'-tetraacetic acid

(EGTA) was added. Hybridization was carried out at  $60^{\circ}$ C for 10 min, followed by addition of 300  $\mu$ l of 0.6 M sodium borate pH 8.5, 1% Triton X-100 and a second incubation at  $60^{\circ}$ C for 6 min to hydrolyze the AE on unhybridized probe. Samples were cooled in ice water for 1 min, placed at room temperature for another 3 min, and then analyzed in a LEADER 1 luminometer equipped with automatic injection of detection reagent I (containing 0.1% hydrogen peroxide and 1 mM nitric acid) and detection reagent II (containing 1 N sodium hydroxide and a surfactant component). Some of the hybridization reactions were enhanced with the addition of 4 pmol of unlabelled "helper probe" as disclosed in Hogan et al., U.S. Patent No. 5,030,557 entitled "Means and Methods for Enhancing Nucleic Acid Hybridization", hereby incorporated by reference herein. An RLU value greater than 5,000 RLU was a positive result; less than 5,000 RLU was a negative result.

The following data (Table 1) show that the probes do not cross react with viral DNA from closely related viruses found in human blood or tissues. The samples also gave a positive signal when tested with a probe specific to each target, thereby confirming sample adequacy.

		<u>Table</u>	1. Hybr	idization	Assay W	ith HIV-1 p	robes.	
	Target:	1	2	3	4	5	6	7
20	Probe							
	Sequence	2						
	ID No:							
	1	179,166	482	500	496	190	496	470
25	2	14,992	563	394	377	409	383	465
23	4	61,691	2,818	750	695	686	702	642
	6	28,038	546	408	375	356	369	372
	7	27,407	640	401	252	366	343	359
30	8	45,868	1,432	395	392	386	401	404
30	9	15,971	721	280	268	26 <b>1</b>	274	284
	10	59,007	714	264	280	284	272	567
	11	25,856	4,641	3,598	3,736	3,711	3,855	3,388
35	12	140,691	1,846	602	694	531	534	1,236
		Target 1 = H	IV-1 BH	10 isolat	e 9 Kb <u>S</u>	<u>stI</u> fragmen	t, Target	. 2
		= Human Immu	nodefic	iency Vir	us Type	2 (NIHZ iso	late) 9 K	(b
		Nael fragmen	t, Targ	et 3 = Hu	ıman T-ce	ll leukemia	virus ty	/pe
40		1 (pMT-2) 5'	4.6 Kb	SstI-Bam	<u>HI</u> fragm	ent; Target	4 = Huma	ŧn
T-cell leukemia virus type 1 3' 4.4 Kb <u>XbaI-SstI</u>						<u>I</u> fragmen	it,	

Target 5 = Human T-cell leukemia virus type 2 3.5 Kb <u>BamHI</u> fragment, Target 6 = Human T-cell leukemia virus type 2 5 Kb <u>BamHI</u> fragment, Target 7 = Human Hepatitis B virus serotype ADW 1.3, 1.8 Kb <u>BamHI</u> fragments.

The above data confirm that the novel probes herein disclosed and claimed are capable of distinguishing Human Immunodeficiency Virus type 1 from these viruses found in human blood.

## Example 2. Amplification of HIV by PCR

To demonstrate the reactivity of the primers and probes for Human Immunodeficiency Virus type 1, the following experiment was performed. Zero, 20, or 100 copies of plasmid DNA containing Human Immunode-

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ficiency Virus DNA was linearized with a restriction endonuclease, and added to amplification reactions containing 50 pmol of each primer, 10 mM Tris HCl pH 8, 50 mM KCl, 1.25 mM MgCl<sub>2</sub>, 0.25 mM each of dATP, dTTP, dCTP, dGTP, and 2.5 U Taq DNA polymerase in 50 μl. The reactions were incubated at 95°C for 1-2 min, and then cycled 35 times at 55°C for 15 sec, 72°C for 30 sec, and 95°C for 20 sec in a Perkin-Elmer 9600 thermocycler or 55°C for 30 sec, 72°C for 60 sec, and 95°C for 60 sec in a Perkin-Elmer 48 well thermocycler. Following cycling, the reactions were incubated at 72°C for 6-7 min and stored at 4°C. Ten μl of the product was analyzed by hybridization protection assay with 0.04 pmol of labeled probe. The data are shown in Table 2. RLU greater than 7,000 is considered a positive result.

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Table 2. Amplification of Human Immunodeficiency Virus Type 1 by PCR

15				Sample	RLU
	•		0 с	20 c	100 c
	Primer	Pro	be		
	Sequence	Seq	uence		
20	ID Nos:	ID.	No.		
	19/20*	1	886	827,202	723,008
	21/22*	2	2,677	24,030	48,521
	<b>*</b> 23/25	3	370	144,082	603,456
25	*24/27	4	4,042	81,052	163,355
	*26/28	5	263	273,023	593,022
	*29/30	6	1,008	328,736	366,590
	*31/32	7	3,394	73,690	86,168
30	*33/34	8	1,648	7,152	24,027
	*35/36	9	560	82,980	145,681
	*39/40	10	810	279,079	299,815
	*39/41	10	886	362,914	427,500
35	42/43*	11	5,830	680,788	1,939,372
-	*44/45	12	1,387	21,428	130,709

The starred (\*) primers had the sequence 5'AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end'of
the primer. 0 c = 0 copies of HIV DNA, 20 c = 20 copies of
HIV DNA, 100 c = 100 copies of HIV DNA. Probe 1 was used
in the presence of unlabeled helper probe SEQ. ID. No. 15.
Probe 7 was used in the presence unlabeled helper probe
SEQ. ID. No. 16. Probe 10 was used in the presence of
unlabeled helper probe SEQ. ID. No. 17. Probe 12 was used
in the presence of unlabeled helper probe SEQ. ID. No. 18.
As the copy number increased, RLU increased. Thus, the
primers of the present invention were able to successfully
amplify, by PCR, HIV type 1 target sequences which were
detected using the probes of the present invention.

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### Example 3. Patient samples

In this example, patient samples containing lysate prepared from 200,000 Ficoll-Hypaque purified white blood cells from individuals known to be infected with HIV type 1 or an individual not infected with HIV type 1 (negative) were analyzed as described in Example 2. These cells were prepared as described in Ryder and Kacian, entitled "Preparation of nucleic acid from blood," U.S. Serial number 07/898,785, filed 6/12/92. The results are shown in Table 3.

10			Table 3.	PCR Assay	
			Sample	RLU	
15			Patient 1	Patient 2	Negative
	Primer	Probe			
	Sequence	Sequence			
20	ID Nos:	ID. No.			
	19/20*	1	27,616	71,981	886
	21/22*	2	34,949	35,483	565
05	*23/25	3	45,230	93,529	455
25	*24/27	4	2,355	25,329	1,052
	<b>*</b> 26/28	5	22,345	26,014	369
	*31/32	7	200,418	130,486	481
30	*3 <b>3</b> /34	8	43,993	40,389	705
	*39/40	10	36,310	50,838	976
	<b>*</b> 39/41	10	55,582	98,504	993
35	42/43*	11	99,028	207,605	6,057
30	*44/45	12	55,082	80,388	1,496

The starred (\*) primers had the sequence 5'AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end of
the primer. The primers of the present invention were able

to amplify by PCR HIV type 1 target sequences present in individuals infected with HIV. The amplified target sequences were detected by the probes of the present invention. Thus, individuals containing HIV type 1 and an individual not containing HIV type 1 were correctly identified.

### Example 4. Non-PCR Amplification

To show that the amplification oligomers also work in a transcription based amplification assay, 0, 2,000, or 20,000 copies of plasmid DNA containing HIV type 1 was linearized using a restriction endonuclease, and heated to 95°C for two min and cooled to 37°C for 1 min. Following addition of 800 U of MMLV reverse transcriptase the reactions were incubated for 12 min at 37°C, heated to 95°C for two min, and cooled to 37°C for

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one min. 800 U of MMLV reverse transcriptase and 400 U of T7 RNA polymerase were added and the reactions were incubated for 3 hr at 37°C. The final amplification conditions were 70 mM Tris HCl, pH 8, 35 mM KCl, 15 mM KOH neutralized N-acetyl-cysteine, 6 mM rGTP, 4 mM rCTP, 4 mM rATP, 4 mM rUTP, 1 mM each of dTTP, dATP, dCTP and dGTP, and 22 mM MgCl $_2$  in 100  $\mu$ l. Ten  $\mu$ l of each reaction was mixed with 40  $\mu$ l of water and assayed as described for Table 1 except that the hybridization buffer contained 20 mM aldrithiol. The results in RLU are shown in Table 4.

Table 4. Transcription-Based Amplification Assay

RLU

	Primers	Probe	0 C	2,000 c	20,000 c
15	Sequence	Sequence	9		
	ID Nos:	ID. No.			
	19/20*	1	681	24,170	190,536
20	21/22*	2	793	62,476	523,770
	*23/25	3	2,239	812,577	1,126,045
	*24/27	4	1,901	160,274	780,351
25	*26/28	. 5	2,555	877,893	1,167,756
	*29/30	6	868	299,255	880,119
	*31/32	7	871	129,732	969,034
	*33/34	8	710	134,887	986,266
30	*35/36	9	884	128,981	1,021,865
	*39/40	10	1,597	375,629	478,883
	*39/41	10	1,264	499,304	495,509
	*44/45	12	2,426	41,684	542,339

The starred (\*) primers had the sequence 5'
AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end of
the primer. Probe 1 was used in the presence of unlabelled
helper probe SEQ. ID. No. 15. Probe 7 was used in the
presence of unlabelled helper probe SEQ. ID. No. 16, probe
10 was used in the presence of unlabelled helper probe SEQ.
ID. No. 17, and probe 12 was used in the presence of
unlabelled helper probe SEQ. ID. No. 18. 0 c = 0 copies of
HIV DNA, 2,000 c = 2,000 copies of HIV DNA, 20,000 c =
20,000 copies of HIV DNA.

As the copy number increased RLU also increased. Thus, the primers of the present invention can be used to amplify HIV type 1 target sequences using a transcription based amplification assay and the amplified target sequences can be detected using the probes of the present invention.

## Example 5.

This example demonstrates the ability of probes for Human Immunodeficiency Virus type 1 to detect low-levels of target oligomer produced in a transcription based amplification assay. Zero or 10 copies of plasmid

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DNA containing HIV type I sequence was linearized using a restriction endonuclease, heated in the presence of 1  $\mu$ g of human DNA to 95°C for eight minutes, and then cooled to 42°C for six minutes. Amplification was carried out at 42°C for two hours using 800 U MMLV reverse transcriptase and 400 U of T7 RNA polymerase, in the following reaction mix: 50 mM Tris HCl pH 8, 17.5 mM MgCl<sub>2</sub>, 0.05 mM zinc acetate, 10% glycerol, 6.25 mM rGTP, 2.5 mM rCTP, 6.25 mM rATP, 2.5 mM rUTP, 0.2 mM dTTP, 0.2 mM dATP, 0.2 mM, 0.2 mM dCTP and 0.2 mM dGTP. Primer SEQ ID NOs. 26, 28, and 41 were used at a concentration of 30 pmol, primer SEQ ID NO. 39 was used at a concentration of 15 pmol. The entire reaction was analyzed using the hybridization protection assay with 0.04 pmol of probe in 100  $\mu$ l of the hybridization buffer (supplemented with 20 mM aldrithiol) as described in Example 1. Probe SEQ ID NO. 10 was hybridized in the presence of 2 pmol unlabeled helper SEQ ID NO. 17.

Table 5. Low Level Transcription-Based Amplification Assay

15			RLU	
	Primers SEQ	Probe SEQ	0 copies	10 copies
	ID NOs.			
20	*26/28	5	1,293	64,639
	*39/40	10	2,143	564,185

The 10 copy values represent the average of ten replicates.

The starred (\*) primers had the sequence 5'
AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end of the primer.

Other embodiments are within the following sequence listing.

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(ii) TITLE OF INVENTION: NUCLEIC ACID AMPLIFICATION OLIGONUCLEOTIDES AND PROBES 10 TO HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 (iii) NUMBER OF SEQUENCES: 140 (iv) CORRESPONDENCE ADDRESS: 15 Lyon & Lyon (A) ADDRESSEE: 611 West Sixth Street (B) STREET: Los Angeles (C) CITY: California (D) STATE: USA (E) COUNTRY: 20 90017 (F) ZIP: (v) COMPUTER READABLE FORM: 3.5" Diskette, 1.44 Mb storage (A) MEDIUM TYPE: 25 IBM PS/2 Model 50Z or 55SX (B) COMPUTER: IBM P.C. DOS (Version 3.30) (C) OPERATING SYSTEM: WordPerfect (Version 5.0) (D) SOFTWARE: (vi) CURRENT APPLICATION DATA: 30 (A) APPLICATION NUMBER: (B) FILING DATE: (C) CLASSIFICATION: (vii) PRIOR APPLICATION DATA: 35 Prior applications total, including application described below: 2 U.S. Serial No. 07/550,837 (A) APPLICATION NUMBER: 40 (B) FILING DATE: 7/10/90 U.S. Serial No. 07/379,501 (A) APPLICATION NUMBER: 45 7/11/89 (B) FILING DATE: 50

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(1) APPLICANT.

5	(viii) ATTO	RNEY/AGENT INFORMATION:	
	(B)	NAME: REGISTRATION NUMBER: REFERENCE/DOCKET NUMBER	
10	(ix) TELECO	MMUNICATION INFORMATION:	:
	(B)	TELEPHONE: TELEFAX: TELEX:	(213) 489-1600 (213) 955-0440 67-3510
15	(2) INFORMATION FOR	SEQ ID NO: 1:	
	(i) SEQUENC	E CHARACTERISTICS:	
20	(B) (C)	LENGTH: TYPE: STRANDEDNESS: TOPOLOGY:	31 nucleic acid single linear
	(ii) SEQUEN	CE DESCRIPTION : SEQ ID	NO: 1:
	GACTAGCGGA GGCTAGAAG	G AGAGAGATGG G 31	
25	(3) INFORMATION FOR	SEQ ID NO: 2:	
	(i) SEQUENCE	E CHARACTERISTICS:	
30	(B) (C)	LENGTH: TYPE: STRANDEDNESS: TOPOLOGY:	31 nucleic acid single linear
	(ii) SEQUENC	CE DESCRIPTION : SEQ ID	NO: 2:
35	GAAGGCTTTC AGCCCAGAAG	G TAATACCCAT G 31	
	(4) INFORMATION FOR S	SEQ ID NO: 3:	
	(i) SEQUENCE	CHARACTERISTICS:	·
40	(B) (C)	LENGTH: TYPE: STRANDEDNESS: TOPOLOGY:	30 nucleiç acid single linear
	(ii) SEQUENC	E DESCRIPTION : SEQ ID	NO: 3:
45	ATTTGCATGG CTGCTTGATG	TCCCCCACT	30

50

5	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 26 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 4:
	CTTCCCCTTG GTTCTCTCAT CTGGCC 26
15	(6) INFORMATION FOR SEQ ID NO: 5:
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 37 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 5:
25	GTCATCCATC CTATTTGTTC CTGAAGGGTA CTAGTAG 37
	(7) INFORMATION FOR SEQ ID NO: 6:
30	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 33 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 6:
	CTCCCTGACA TGCTGTCATC ATTTCTTCTA GTG 33
40	(8) INFORMATION FOR SEQ ID NO: 7:
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 31 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
50	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 7:

	GTGGAAGCAC ATTGTACTGA TATCTAATCC C	31	
	(9) INFORMATION FOR SEQ ID NO: 8	:	
5	(i) SEQUENCE CHARACTERISTIC	cs:	
10	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>		37 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID	NO: 8:
15	GCTCCTCTAT TTTTGTTCTA TGCTGCCCTA TT	TCTAA	37
10	(10) INFORMATION FOR SEQ ID NO:	9:	
	(i) SEQUENCE CHARACTERISTIC	cs:	
20	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>		23 nucleic acid single linear
25	(ii) SEQUENCE DESCRIPTION	: SEQ ID	NO: 9:
	CCTTTGTGTG CTGGTACCCA TGC 23		
	(11) INFORMATION FOR SEQ ID NO:	10:	
30	(i) SEQUENCE CHARACTERISTIC	cs:	
35	<pre>(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:</pre>		nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID	NO: 10:
	CTACTATTCT TTCCCCTGCA CTGTACCCC	29	
40	(12) INFORMATION FOR SEQ ID NO:	11:	
	(i) SEQUENCE CHARACTERISTIC	cs:	
45	<pre>(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:</pre>		29 nucleic acid single linear
50			

	(it) CROVENCE DESCRIPTION . SEO ID NO. 11.
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 11:
5	AAAGCCTTAG GCATCTCCTA TGGCAGGAA 29
	(13) INFORMATION FOR SEQ ID NO: 12:
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 28 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
15	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 12:
	GCAGCTGCTT ATATGCAGGA TCTGAGGG 28
	(14) INFORMATION FOR SEQ ID NO: 13:
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 33 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 13:
20	CAAGGCAAGC TTTATTGAGG CTTAAGCAGT GGG 33
30	(15) INFORMATION FOR SEQ ID NO: 14:
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 28 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
40	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 14:
	ATCTCTAGCA GTGGCGCCCG AACAGGGA 28
	(16) INFORMATION FOR SEQ ID NO: 15:
45	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 24 (B) TYPE: nucleic acid (C) STRANDEDNESS: single

	(I	O) TOPOLOGY:	linear	
	(ii) SEQUE	ENCE DESCRIPTION	: SEQ ID NO: 15:	
5	TGCGAGAGCG TCAGTATT	TAA GCGG	24	
	(17) INFORMATION FO	OR SEQ ID NO:	16:	
10	(i) SEQUEN	NCE CHARACTERISTI	cs:	
_	() ()	A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:	36 nuclei single linear	c acid
15	(ii) SEQUE	ENCE DESCRIPTION	: SEQ ID NO: 16:	
	CTACTTTGGA ATATTGCT	GG TGATCCTTTC CA	TCCC 36	
20	(18) INFORMATION FO	OR SEQ ID NO:	17:	
	(i) SEQUEN	NCE CHARACTERISTI	cs:	
25	(E	A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:	33 nuclei single linear	c acid
	(ii) SEQUE	ENCE DESCRIPTION	: SEQ ID NO: 17:	
30	CCAATCCCCC CTTTTCTT	TTT AAAATTGTGG AT	G 33	
	(19) INFORMATION FO	OR SEQ ID NO:	18:	
35	(i) SEQUEN	NCE CHARACTERISTI	cs:	
	(E	A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:	24 nuclei single linear	c acid
40	(ii) SEQUE	ENCE DESCRIPTION	: SEQ ID NO: 18:	
	CTCGCCACTC CCCAGTCC	CCG CCCA	24	
45	(20) INFORMATION FO	OR SEQ ID NO:	19:	
	(i) SEQUEN	CE CHARACTERISTI	cs:	
	( 2	A) LENGTH:	24	
50				•

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5	(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 19:
	CTCGACGCAG GACTCGGCTT GCTG	24
10	(21) INFORMATION FOR SEQ ID NO:	20:
	(i) SEQUENCE CHARACTERIST	cs:
15	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	23 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 20:
20	CTCCCCCGCT TAATACTGAC GCT	23
	(22) INFORMATION FOR SEQ ID NO:	21:
25	(i) SEQUENCE CHARACTERIST	ics:
30	<pre>(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:</pre>	31 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 21:
	GGCAAATGGT ACATCAGGCC ATATCACCTA G	31
35	(23) INFORMATION FOR SEQ ID NO:	22:
	(i) SEQUENCE CHARACTERIST	ics:
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	25 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 22: .
45	GGGGTGGCTC CTTCTGATAA TGCTG	25
	(24) INFORMATION FOR SEQ ID NO:	23:
50	(i) SEQUENCE CHARACTERIST	ics:

5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	26 nucleic acid single lin ar
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 23:
10	CAGAAGGAGC CACCCCACAA GATTTA	26
,	(25) INFORMATION FOR SEQ ID NO:	24:
	(i) SEQUENCE CHARACTERIST	ICS:
15	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	27 nucleic acid single linear
20	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 24:
	GACCATCAAT GAGGAAGCTG CAGAATG	27
	(26) INFORMATION FOR SEQ ID NO:	25:
25	(i) SEQUENCE CHARACTERIST	rics:
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	25 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 25:
35	CCCATTCTGC AGCTTCCTCA TTGAT	25
33	(27) INFORMATION FOR SEQ ID NO:	26:
	(i) SEQUENCE CHARACTERIST	TICS:
40	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	19 nucleic acid single linear
45	(ii) SEQUENCE DESCRIPTION	N : SEQ ID NO: 26:
	AGTGACATAG CAGGAACTA 19	
50	(28) INFORMATION FOR SEQ ID NO:	27:

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	(i) SEQUENCE CHARACTERIST	cs:
5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	26 nucleic acid single linear
10	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 27:
, ,	CCATCCTATT TGTTCCTGAA GGGTAC	26
	(29) INFORMATION FOR SEQ ID NO:	28:
15	(i) SEQUENCE CHARACTERIST	ics:
20	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	23 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 28:
	AGATTTCTCC TACTGGGATA GGT	23
25	(30) INFORMATION FOR SEQ ID NO:	29:
	(i) SEQUENCE CHARACTERIST	ics:
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	30 nučleic acid single linear
35	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 29:
	GAAACCTTGT TGAGTCCAAA ATGCGAACCC	30
40	(31) INFORMATION FOR SEQ ID NO:	30:
40	(i) SEQUENCE CHARACTERIST	ics:
45	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	18 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 30:
50		

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	TGTGCCCTTC TTTGCC	AC 18		
	(32) INFORMATION	FOR SEQ ID NO:	31:	
5	(i) SEQU	IENCE CHARACTERIST	cics:	
10		(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:		22 nucleic acid single linear
	(ii) SEQ	QUENCE DESCRIPTION	: SEQ ID	NO: 31:
15	CAGTACTGGA TGTGGG	GTGAT GC 22		
	(33) INFORMATION	FOR SEQ ID NO:	32:	
	(i) SEQU	JENCE CHARACTERIST	rics:	
20		(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:		35 nucleic acid single linear
25	(ii) SEQ	QUENCE DESCRIPTION	seQ ID	NO: 32:
	GTCATGCTAC TTTGGA	AATAT TTCTGGTGAT	CCTTT	35
	GTCATGCTAC TTTGGA		33:	35
30	(34) INFORMATION		33:	35
30 35	(34) INFORMATION (i) SEQU	FOR SEQ ID NO:  JENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	33: rics: :	33 nucleic acid single linear
	(34) INFORMATION (i) SEQU	FOR SEQ ID NO:  JENCE CHARACTERIST  (A) LENGTH:  (B) TYPE:  (C) STRANDEDNESS:	33: TICS: : N : SEQ ID	33 nucleic acid single linear
	(34) INFORMATION (i) SEQU	FOR SEQ ID NO:  JENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS (D) TOPOLOGY:  QUENCE DESCRIPTION	33: TICS: : N : SEQ ID	33 nucleic acid single linear
35	(34) INFORMATION (i) SEQUAL (ii) SEQUAL (ii) SEQUAL (iii)	FOR SEQ ID NO:  JENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS (D) TOPOLOGY:  QUENCE DESCRIPTION	33: FICS:  SEQ ID  GAC 33	33 nucleic acid single linear
35	(34) INFORMATION (i) SEQUAL (ii) SEQUAL (ii) SEQUAL (iii)	FOR SEQ ID NO:  JENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  QUENCE DESCRIPTION  TTGTA TGTAGGATCT (C)  FOR SEQ ID NO:	33: FICS:  SEQ ID  GAC 33  34: TICS:	33 nucleic acid single linear

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(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 34:
     ACCAAAGGAA TGGAGGTTCT TTCTGATG
                                                     28
5
      (36) INFORMATION FOR SEQ ID NO:
                                          35:
               (i) SEQUENCE CHARACTERISTICS:
                                                     28
10
                       (A) LENGTH:
                                                     nucleic acid
                        (B) TYPE:
                                                     single
                        (C) STRANDEDNESS:
                                                     linear
                        (D) TOPOLOGY:
               (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 35:
15
      GCATTAGGAA TCATTCAAGC ACAACCAG
      (37) INFORMATION FOR SEQ ID NO:
                                          36:
20
                (i) SEQUENCE CHARACTERISTICS:
                                                     34
                        (A) LENGTH:
                                                     nucleic acid
                        (B) TYPE:
                                                     single
                        (C) STRANDEDNESS:
25
                                                     linear
                        (D) TOPOLOGY:
                (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 36:
      GCACTGACTA ATTTATCTAC TTGTTCATTT CCTC
                                                      34
30
      (38) INFORMATION FOR SEQ ID NO:
                (i) SEQUENCE CHARACTERISTICS:
                                                      38
35
                        (A) LENGTH:
                                                      nucleic acid
                        (B) TYPE:
                                                      single
                        (C) STRANDEDNESS:
                                                      linear
                         (D) TOPOLOGY:
                (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 37:
40
       GGGATTGGAG GAAATGAACA AGTAGATAAA TTAGTCAG
                                                           38
       (39) INFORMATION FOR SEQ ID NO:
45
                 (i) SEQUENCE CHARACTERISTICS:
                         (A) LENGTH:
                                                    nucleic acid
                         (B) TYPE:
                                                     single
                         (C) STRANDEDNESS:
50
```

	(D) TOPOLOGY:		linear
5	(ii) SEQUENCE DESCRIPTION	: SEQ ID	No: 38:
	TGTGTACAAT CTAGTTGCCA TATTCCTGGA C	TACA	35
	(40) INFORMATION FOR SEQ ID NO:	39:	
10	(i) SEQUENCE CHARACTERIST	ics:	
15	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:		22 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID	NO: 39:
	CAAATGGCAG TATTCATCCA CA	22	·
20	(41) INFORMATION FOR SEQ ID NO:	40:	
	(i) SEQUENCE CHARACTERIST	ics:	
25	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:		23 nucleic acid single linear
30	(ii) SEQUENCE DESCRIPTION	: SEQ ID	NO: 40:
	GTTTGTATGT CTGTTGCTAT TAT	23	•
	(42) INFORMATION FOR SEQ ID NO:	41:	
35	(i) SEQUENCE CHARACTERIST	ics:	
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:		18 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID	NO: 41:
	CCCTTCACCT TTCCAGAG	18	
45	(43) INFORMATION FOR SEQ ID NO:	42:	
	(i) SEQUENCE CHARACTERIST	ics:	
50	(A) LENGTH:		27

5	(B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 42:
	GAGCCCTGGA AGCATCCAGG AAGTCAG 27
10	(44) INFORMATION FOR SEQ ID NO: 43:
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 21 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
20	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 43:
20	CTTCGTCGCT GTCTCCGCTT C 21
	(45) INFORMATION FOR SEQ ID NO: 44:
25	(i) SEQUENCE CHARACTERISTICS:
30	(A) LENGTH: 27 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 44:
	CAAGGGACTT TCCGCTGGGG ACTTTCC 27
35	(46) INFORMATION FOR SEQ ID NO: 45:
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 27 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 45:
45	GTCTAACCAG AGAGACCCAG TACAGGC 27
	(47) INFORMATION FOR SEQ ID NO: 46:
50	(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	25 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	N : SEQ ID NO: 46:
	GTACTGGGTC TCTCTGGTTA GACCA	25
10	(48) INFORMATION FOR SEQ ID NO:	47:
	(i) SEQUENCE CHARACTERIST	rics:
15	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	28 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 47:
20	CACACAACAG ACGGGCACAC ACTACTTG 28	
	(49) INFORMATION FOR SEQ ID NO:	48:
25	(i) SEQUENCE CHARACTERIST	rics:
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	25 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 48:
	CTGAGGGATC TCTAGTTACC AGAGT	25 .
35	(50) INFORMATION FOR SEQ ID NO:	49:
	(i) SEQUENCE CHARACTERIST	ics:
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	23 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 49:
45	CTCTGGTAAC TAGAGATCCC TCA	23
	(51) INFORMATION FOR SEQ ID NO:	50:
50		

	(i) SEQUENCE CHARACTERIST	ics:
5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	23 nucleic acid single linear
10	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 50:
	GTTCGGGCGC CACTGCTAGA GAT	23
	(52) INFORMATION FOR SEQ ID NO:	51:
15	(i) SEQUENCE CHARACTERIST	ICS:
20	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	23 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 51:
	GCAAGCCGAGT CCTGCGTCG AGA 2:	3
25	(53) INFORMATION FOR SEQ ID NO:	52:
	(i) SEQUENCE CHARACTERIST	ics:
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	27 nucleic acid single linear
35	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 52:
00	AATTTAATAC GACTCACTAT AGGGAGA	27
	(54) INFORMATION FOR SEQ ID NO:	53:
40	(i) SEQUENCE CHARACTERISTI	ics:
<b>4</b> 5	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	31 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 53:
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	CCCATCTCTC TCCTTCTAGC CTCCGCTAGT	C 31
_	(55) INFORMATION FOR SEQ ID NO:	54:
5	(i) SEQUENCE CHARACTERIST	TICS:
	(A) LENGTH: (B) TYPE:	31 nucleic acid
10	(C) STRANDEDNESS: (D) TOPOLOGY:	
	(ii) SEQUENCE DESCRIPTION	Tilledi
15	CATGGGTATT ACTTCTGGGC TGAAAGCCTT (	C 31
	(56) INFORMATION FOR SEQ ID NO:	55:
	(i) SEQUENCE CHARACTERIST	TICS:
20	(A) LENGTH:	30
	(B) TYPE: (C) STRANDEDNESS:	nucleic acid : single
	(D) TOPOLOGY:	linear
25	(ii) SEQUENCE DESCRIPTION	N : SEQ ID NO: 55:
	AGTGGGGGA CATCAAGCAG CCATGCAAAT	30
	AGTGGGGGA CATCAAGCAG CCATGCAAAT (57) INFORMATION FOR SEQ ID NO:	
30		56: PICS:
30	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH:	56: PICS:
	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST	56: PICS: 26 nucleic acid
<i>30</i>	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH: (B) TYPE:	56: PICS: 26 nucleic acid
	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH:  (B) TYPE:  (C) STRANDEDNESS:	56: PICS:  26 nucleic acid single linear
	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH:  (B) TYPE:  (C) STRANDEDNESS:  (D) TOPOLOGY:	56:  PICS:  26  nucleic acid single linear  N: SEQ ID NO: 56:
35	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION	56:  PICS:  26  nucleic acid single linear  N: SEQ ID NO: 56:
35	(i) SEQUENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION  GGCCAGATGA GAGAACCAAG GGGAAG	56:  PICS:  26  nucleic acid single linear  N: SEQ ID NO: 56:  26  57:
35	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION  GGCCAGATGA GAGAACCAAG GGGAAG  (58) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH:	56:  26 nucleic acid single linear  N: SEQ ID NO: 56:  26 57: CICS:
35 40	(i) SEQUENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION  GGCCAGATGA GAGAACCAAG GGGAAG  (58) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST	26 nucleic acid single linear N: SEQ ID NO: 56: 26 57: CICS:
35 40	(57) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION  GGCCAGATGA GAGAACCAAG GGGAAG  (58) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST  (A) LENGTH: (B) TYPE:	56:  TICS:  26 nucleic acid single linear  N: SEQ ID NO: 56:  26 57: TICS:  37 nucleic acid

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	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 57:
	CTACTAGTAC CCTTCAGGAA CAAATAGGAT GGATGAC 37
5	(59) INFORMATION FOR SEQ ID NO: 58:
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 33 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
15	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 58:
75	CACTAGAAGA AATGATGACA GCATGTCAGG GAG 33
	(60) INFORMATION FOR SEQ ID NO: 59:
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 31 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 59:
	GGGATTAGAT ATCAGTACAA TGTGCTTCCA C 31
30	(61) INFORMATION FOR SEQ ID NO: 60:
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 37 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
40	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 60:
	TTAGAAATAG GGCAGCATAG AACAAAAATA GAGGAGC 37
	(62) INFORMATION FOR SEQ ID NO: 61:
45	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 23 (B) TYPE: nucleic acid (C) STRANDEDNESS: single

	(D) TOPOLOGY:	linear
	(ii) SEQUENCE DESCRIPTION :	: SEQ ID NO: 61:
5	GCATGGGTAC CAGCACAA AGG	23
	(63) INFORMATION FOR SEQ ID NO:	52:
10	(i) SEQUENCE CHARACTERISTIC	cs:
	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	29 nucleic acid single linear
15	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 62:
	GGGGTACAGT GCAGGGGAAA GAATAGTAG	29
20	(64) INFORMATION FOR SEQ ID NO:	63:
	(i) SEQUENCE CHARACTERISTIC	cs:
25	<pre>(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:</pre>	29 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 63:
30	TTCCTGCCAT AGGAGATGCC TAAGGCTTT	29
35	(65) INFORMATION FOR SEQ ID NO:	64:
33	(i) SEQUENCE CHARACTERISTIC	cs:
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	28 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 64:
45	CCCTCAGATC CTGCATATAA GCAGCTGC	28
-	(66) INFORMATION FOR SEQ ID NO:	65:
	(i) SEQUENCE CHARACTERISTI	cs:
50		

5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	33 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 65:
	CCCACTGCTT AAGCCTCAAT AAAGCTTGCC TTG	33
10	(67) INFORMATION FOR SEQ ID NO: 66:	
	(i) SEQUENCE CHARACTERISTICS:	
15	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	28 nucleic acid single linear
20	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 66:
20	TCCCTGTTCG GGCGCCACTG CTAGAGAT 2	8
	(68) INFORMATION FOR SEQ ID NO: 67:	
25	(i) SEQUENCE CHARACTERISTICS:	
30	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	31 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 67:
	GACUAGCGGA GGCUAGAAGG AGAGAGAUGG G 3	1
35	(69) INFORMATION FOR SEQ ID NO: 68:	
	(i) SEQUENCE CHARACTERISTICS:	
40	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	31 nucleic acid single linear
45	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 68:
	GAAGGCUUUC AGCCCAGAAG UAAUACCCAU G 3	1
50	(70) INFORMATION FOR SEQ ID NO: 69:	

	(i) SEQUENCE CHARACTERIST	ics:			
5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:			30 nucleic single linear	acid
40	(ii) SEQUENCE DESCRIPTION	: SEQ	ID	NO: 69:	
10	AUUUGCAUGG CUGCUUGAUG UCCCCCACU			30	
	(71) INFORMATION FOR SEQ ID NO:	70:			
15	(i) SEQUENCE CHARACTERIST	ics:			
20	<pre>(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:</pre>			26 nucleic single linear	acid
	(ii) SEQUENCE DESCRIPTION	: SEQ	ID	NO: 70:	
	CUUCCCCUUG GUUCUCUCAU CUGGCC	26			
25	(72) INFORMATION FOR SEQ ID NO:	71:			
	(i) SEQUENCE CHARACTERIST	ics:			
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:			37 nucleic single linear	acid
35	(ii) SEQUENCE DESCRIPTION	: SEQ	·ID	NO: 71:	
	GUCAUCCAUC CUAUUUGUUC CUGAAGGGUA C	UAGUAG		37	
	(73) INFORMATION FOR SEQ ID NO:	72:			
40	(i) SEQUENCE CHARACTERIST	ics:	-		
45	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:			33 nucleiç single linear	acid
	(ii) SEQUENCE DESCRIPTION	: SEQ	ID	NO: 72:	
50	CUCCCUGACA UGCUGUCAUC AUUUCUUCUA G	UG		33	

(74) INFORMATION FOR SEQ ID NO: 73:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 73:

GUGGAAGCAC AUUGUACUGA UAUCUAAUCC C 31

(75) INFORMATION FOR SEQ ID NO: 74:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

GCUCCUCUAU UUUUGUUCUA UGCUGCCCUA UUUCUAA 37

(76) INFORMATION FOR SEQ ID NO: 75:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 75:

CCUUUGUGUG CUGGUACCCA UGC 23

(77) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single (D) TOPOLOGY: linear

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(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 76:

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	CUACUAUUCU UUCCCCUC	GCA CUGUACCCC	29			
	(78) INFORMATION FO	OR SEQ ID NO:	77:			
5	(i) SEQUE	NCE CHARACTERIST	ics:			
10	(1 (0	A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:		29 nucleic acid single linear		
	(ii) SEQU	ENCE DESCRIPTION	: SEQ ID	NO: 77:		
15	AAAGCCUUAG GCAUCUC	CUA UGGCAGGAA	29			
	(79) INFORMATION FO	OR SEQ ID NO:	78:			
	(i) SEQUENCE CHARACTERISTICS:					
20	· (1	A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:		28 nucleic acid single linear		
25	(ii) SEQU	ENCE DESCRIPTION	: SEQ ID	NO: 78:		
	• •					
	GCAGCUGCUU AUAUGCA	GGA UCUGAGGG	28			
30	• •		28 79:			
30	GCAGCUGCUU AUAUGCA		79:	•		
30 35	GCAGCUGCUU AUAUGCAG (80) INFORMATION FG (i) SEQUE	OR SEQ ID NO:	79:	33 nucleic acid single linear		
	GCAGCUGCUU AUAUGCAG (80) INFORMATION FG (i) SEQUE	OR SEQ ID NO:  NCE CHARACTERIST  A) LENGTH:  B) TYPE:  C) STRANDEDNESS:	79: PICS:	nucleic acid single linear		
	GCAGCUGCUU AUAUGCAG (80) INFORMATION FG (i) SEQUE	OR SEQ ID NO:  NCE CHARACTERIST  A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:  ENCE DESCRIPTION	79: ICS:	nucleic acid single linear		
	GCAGCUGCUU AUAUGCAG (80) INFORMATION FG (i) SEQUE (i) (ii) SEQUE	OR SEQ ID NO:  NCE CHARACTERIST  A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:  ENCE DESCRIPTION  AGG CUUAAGCAGU G	79: ICS:	nucleic acid single linear NO: 79:		
35 40	GCAGCUGCUU AUAUGCAG (80) INFORMATION FOR (i) SEQUE (ii) SEQUE (ii) SEQUE CAAGGCAAGC UUUAUUG (81) INFORMATION F	OR SEQ ID NO:  NCE CHARACTERIST  A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:  ENCE DESCRIPTION  AGG CUUAAGCAGU G	79: ICS: I: SEQ ID GG 80:	nucleic acid single linear NO: 79:		
	GCAGCUGCUU AUAUGCAG (80) INFORMATION FOR (i) SEQUE (ii) SEQUE (iii) SEQUE (AAGGCAAGC UUUAUUG (81) INFORMATION FOR (i) SEQUE	OR SEQ ID NO:  NCE CHARACTERIST  A) LENGTH: B) TYPE: C) STRANDEDNESS: D) TOPOLOGY:  ENCE DESCRIPTION  AGG CUUAAGCAGU G  OR SEQ ID NO:	79: ICS: : SEQ ID : GG 80: : ICS:	nucleic acid single linear NO: 79:		

	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 80:
	AUCUCUAGCA GUGGCGCCCG AACAGGGA 28
5	(82) INFORMATION FOR SEQ ID NO: 81:
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH:  (B) TYPE:  (C) STRANDEDNESS:  (D) TOPOLOGY:  31  nucleic acid  single linear
45	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 81:
15 	CCCAUCUCUC UCCUUCUAGC CUCCGCUAGU C 31
	(83) INFORMATION FOR SEQ ID NO: 82:
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 31 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 82:
	CAUGGGUAUU ACUUCUGGGC UGAAAGCCUU C 31
30	(84) INFORMATION FOR SEQ ID NO: 83:
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 31 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
•	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 83:
40	AGUGGGGGA CAUCAAGCAG CCAUGCAAA U 31
	(85) INFORMATION FOR SEQ ID NO: 84:
45	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 (B) TYPE: nucleic acid
50	(C) STRANDEDNESS: single

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	(D) TOPOLOGY:	linear	
5	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 84:	
· ·	GGCCAGAUGA GAGAACCAAG GGGAAG	26	
	(86) INFORMATION FOR SEQ ID NO:	85:	
10	(i) SEQUENCE CHARACTERIST	cics:	
15	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	37 nucleic acid single linear	
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 85:	
	CUACUAGUAC CCUUCAGGAA CAAAUAGGAU G	GGAUGAC 37	
20	(87) INFORMATION FOR SEQ ID NO:	86:	
	(i) SEQUENCE CHARACTERIST	rics:	
25	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	33 nucleic acid single linear	
30	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 86:	
	CACUAGAAGA AAUGAUGACA GCAUGUCAGG G	33 <sub>.</sub>	
	(88) INFORMATION FOR SEQ ID NO:	87:	
35	(i) SEQUENCE CHARACTERIST	rics:	
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	31 nucleic acid single linear	
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 87:	
45	GGGAUUAGAU AUCAGUACAA UGUGCUUCCA C	31	
	(89) INFORMATION FOR SEQ ID NO:	88:	
(i) SEQUENCE CHARACTERISTICS:			
50	(A) LENGTH:	37	

	(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	nucleic acid single linear
5	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 88:
	UUAGAAAUAG GGCAGCAUAG AACAAAAAUA GA	AGGAGC 37
10	(90) INFORMATION FOR SEQ ID NO:	89:
	(i) SEQUENCE CHARACTERIST	ICS:
15	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	23 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 89:
20	GCAUGGGUAC CAGCACAA AGG	23
	(91) INFORMATION FOR SEQ ID NO:	90:
25	(i) SEQUENCE CHARACTERIST	ICS:
	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	29 nucleic acid single linear
30	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 90:
	GGGGUACAGU GCAGGGGAAA GAAUAGUAG	29
35	(92) INFORMATION FOR SEQ ID NO:	91:
	(i) SEQUENCE CHARACTERIST	ICS:
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	29 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 91:
45	UUCCUGCCAU AGGAGAUGCC UAAGGCUUU	29
50	(93) INFORMATION FOR SEQ ID NO:	92:

	(i) SEQUENCE CHARACTERISTICS:	
5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	28 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 92:
10	CCCUCAGAUC CUGCAUAUAA GCAGCUGC 28	
	(94) INFORMATION FOR SEQ ID NO: 93:	•
15	(i) SEQUENCE CHARACTERISTICS:	
	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	33 nucleic acid single linear
20	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 93:
	CCCACUGCUU AAGCCUCAAU AAAGCUUGCC UUG	33
25	(95) INFORMATION FOR SEQ ID NO: 94:	
	(i) SEQUENCE CHARACTERISTICS:	
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	38 nucleic acid single liñear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 94:
35	UCCCUGUUCG GGCGCCACUG CUAGAGAU 38	
	(96) INFORMATION FOR SEQ ID NO: 95:	
40	(i) SEQUENCE CHARACTERISTICS:	
<b>4</b> 5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	24 nucleic acid single. linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 95:
	CCGCTTAATA CTGACGCTCT CGCA 24	

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	(97) INFORMATION FOR SEQ ID NO: 96:
	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 36 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
10	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 96:
	GGGATGGAAA GGATCACCAG CAATATTCCA AAGTAG 36
15	(98) INFORMATION FOR SEQ ID NO: 97:  (i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 33 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 97:
25	CATCCACAAT TTTAAAAGAA AAGGGGGGAT TGG 33
	(99) INFORMATION FOR SEQ ID NO: 98:
20	(i) SEQUENCE CHARACTERISTICS:
30	(A) LENGTH: 24 (B) TYPE: nutleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
35	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 98:
	TGGGCGGAC TGGGGAGTGG CGAG 24
40	(100) INFORMATION FOR SEQ ID NO: 99:
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 24 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
50	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 99:

	CUCGACGCAG GACUCGGCUU GCUG 24	
	(101) INFORMATION FOR SEQ ID NO: 100:	
5	(i) SEQUENCE CHARACTERISTICS:	
10	(A) LENGTH: 23 (B) TYPE: nucle (C) STRANDEDNESS: sing (D) TOPOLOGY: line	
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 1	00:
15	CUCCCCCGCU UAAUACUGAC GCU 23	
,,,	(102) INFORMATION FOR SEQ ID NO: 101:	
	(i) SEQUENCE CHARACTERISTICS:	
20	(A) LENGTH: 31 (B) TYPE: nucle (C) STRANDEDNESS: sing (D) TOPOLOGY: line	
25	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 1	01.
	• • •	01.
	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31	01.
30	!	<b>.</b>
30	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31	
30 35	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31  (103) INFORMATION FOR SEQ ID NO: 102:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25	eic acid le
	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31  (103) INFORMATION FOR SEQ ID NO: 102:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25  (B) TYPE: nucleon (C) STRANDEDNESS: sing	eic acid le ar
	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31  (103) INFORMATION FOR SEQ ID NO: 102:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25  (B) TYPE: nucle (C) STRANDEDNESS: sing (D) TOPOLOGY: line	eic acid le ar
35	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31  (103) INFORMATION FOR SEQ ID NO: 102:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25  (B) TYPE: nucle (C) STRANDEDNESS: sing (D) TOPOLOGY: line  (ii) SEQUENCE DESCRIPTION: SEQ ID NO: 1	eic acid le ar
35	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31  (103) INFORMATION FOR SEQ ID NO: 102:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 (B) TYPE: nucle (C) STRANDEDNESS: sing (D) TOPOLOGY: line  (ii) SEQUENCE DESCRIPTION: SEQ ID NO: 14  GGGGGUGGCUC CUUCUGAUAA UGCUG 25	eic acid le ar
35	GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31  (103) INFORMATION FOR SEQ ID NO: 102:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 (B) TYPE: nucle (C) STRANDEDNESS: sing (D) TOPOLOGY: line  (ii) SEQUENCE DESCRIPTION: SEQ ID NO: 103:  GGGGUGGCUC CUUCUGAUAA UGCUG 25  (104) INFORMATION FOR SEQ ID NO: 103:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 26	eic acid le ar 02: eic acid le

```
CAGAAGGAGC CACCCCACAA GAUUUA 26
     (105) INFORMATION FOR SEQ ID NO: 104:
             (i) SEQUENCE CHARACTERISTICS:
                                                 27
                      (A) LENGTH:
                                                nucleic acid
10
                      (B) TYPE:
                                                single
                      (C) STRANDEDNESS:
                                                linear
                      (D) TOPOLOGY:
              (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 104:
15
     GACCAUCAAU GAGGAAGCUG CAGAAUG
                                        27
     (106) INFORMATION FOR SEQ ID NO: 105:
              (i) SEQUENCE CHARACTERISTICS:
20
                                                  25
                      (A) LENGTH:
                                                 nucleic acid
                      (B) TYPE:
                                                 single
                      (C) STRANDEDNESS:
                                                 linear
                      (D) TOPOLOGY:
25
              (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 105:
     CCCAUUCUGC AGCUUCCUCA UUGAU
30
     (107) INFORMATION FOR SEQ ID NO: 106:
              (i) SEQUENCE CHARACTERISTICS:
                      (A) LENGTH:
35
                                                  nucleic acid
                       (B) TYPE:
                                                  single
                       (C) STRANDEDNESS:
                                                  linear
                      (D) TOPOLOGY:
              (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 106:
 40
     AGUGACAUAG CAGGAACUA 19
     (108) INFORMATION FOR SEQ ID NO: 107:
 45
               (i) SEQUENCE CHARACTERISTICS:
                                                  26
```

55

50

nucleic acid

single

(A) LENGTH:

(C) STRANDEDNESS:

(B) TYPE:

	(D) TOPOLOGY:	linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 107:
5	CCAUCCUAUU UGUUCCUGAA GGGUAC	26
	(109) INFORMATION FOR SEQ ID NO:	108:
10	(i) SEQUENCE CHARACTERIST	ics:
15	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	23 nucleic acid single linear
15	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 108:
	AGAUUUCUCC UACUGGGAUA GGU	23
20	(110) INFORMATION FOR SEQ ID NO:	109:
	(i) SEQUENCE CHARACTERIST	ICS:
25	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	30 nucleic acid single linear
30	(ii) SEQUENCE DESCRIPTION	
	GAAACCUUGU UGAGUCCAAA AUGCGAACCC	•
	(111) INFORMATION FOR SEQ ID NO:	
35	(i) SEQUENCE CHARACTERIST	
	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS:	
40	(D) TOPOLOGY:	linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 110:
45	UGUGCCCUUC UUUGCCAC 18	
	(112) INFORMATION FOR SEQ ID NO:	
	(i) SEQUENCE CHARACTERIST	
50	(A) LENGTH:	22

	<pre>(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:</pre>	nucleic acid single linear
5	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 111:
	CAGUACUGGA UGUGGGUGAU GC 22	
10	(113) INFORMATION FOR SEQ ID NO: 112:	
	(i) SEQUENCE CHARACTERISTICS:	
15		35 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 112:
20	GUCAUGCUAC UUUGGAAUAU UUCUGGUGAU CCUUU	35
	(114) INFORMATION FOR SEQ ID NO: 113:	
25	(i) SEQUENCE CHARACTERISTICS:	
25		33 nucleic acid single linear
30	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 113:
	CAAUACAUGG AUGAUUUGUA UGUAGGAUCU GAC 33	:
35	(115) INFORMATION FOR SEQ ID NO: 114:	,
	(i) SEQUENCE CHARACTERISTICS:	
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	28 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 114;
45	ACCAAAGGAA UGGAGGUUCU UUCUGAUG	28
	(116) INFORMATION FOR SEQ ID NO: 115:	
50	(i) SEQUENCE CHARACTERISTICS:	

5	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	28 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 115:
	GCAUUAGGAA UCAUUCAAGC ACAACCAG 28	
10	1161	
	(117) INFORMATION FOR SEQ ID NO: 116:	
	(i) SEQUENCE CHARACTERISTICS:	
15	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	34 nucleic acid single linear
20	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 116:
	GCACUGACUA AUUUAUCUAC UUGUUCAUUU CCUC	34
	(118) INFORMATION FOR SEQ ID NO: 117:	
25	(i) SEQUENCE CHARACTERISTICS:	
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	38 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 117:
35	GGGAUUGGAG GAAAUGAACA AGUAGAUAAA UUAGUCAG	38
	(119) INFORMATION FOR SEQ ID NO: 118:	•
	(i) SEQUENCE CHARACTERISTICS:	
<b>40</b>	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	35 nucleic acid single, linear
45	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 118:
	UGUGUACAAU CUAGUUGCCA UAUUCCUGGA CUACA	35

	(120) INFORMATION FOR SEQ ID NO:	119:
	(i) SEQUENCE CHARACTERIST	ics:
5	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	22 nucleic acid single linear
10	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 119:
	CAAAUGGCAG UAUUCAUCCA CA	22
15	(121) INFORMATION FOR SEQ ID NO:  (i) SEQUENCE CHARACTERIST:	
20	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	23 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 120:
25	GUUUGUAUGU CUGUUGCUAU UAU	23
	(122) INFORMATION FOR SEQ ID NO:	121:
	(i) SEQUENCE CHARACTERIST	ics:
30	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	18 nucleic acid single linear
35	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 121:
	CCCUUCACCU UUCCAGAG	18
40	(123) INFORMATION FOR SEQ ID NO:	122:
	(i) SEQUENCE CHARACTERISTI	CCS:
45	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	27 nucleic acid single linear
50	(ii) SEQUENCE DESCRIPTION	: SEQ ID NO: 122:

	GAGCCCUGGA AGCAUCCAGG AAGUCAG 27	
	(124) INFORMATION FOR SEQ ID NO: 123:	
5	(i) SEQUENCE CHARACTERISTICS:	
10	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	21 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 123:
15	CUUCGUCGCU GUCUCCGCUU C 21	
	(125) INFORMATION FOR SEQ ID NO: 124:	
,	(i) SEQUENCE CHARACTERISTICS:	
20	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	27 nucleic acid single linear
25	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 124:
	CAAGGGACUU UCCGCUGGGG ACUUUCC 27	
	(126) INFORMATION FOR SEQ ID NO: 125:	
30	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH:	•
35	(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	27 nucleic acid single linear
35	(B) TYPE: (C) STRANDEDNESS:	nucleic acid single linear
35 40	(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	nucleic acid single linear
35	(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION : SEQ ID  GUCUAACCAG AGAGACCCAG UACAGGC 27	nucleic acid single linear
40	(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION : SEQ ID  GUCUAACCAG AGAGACCCAG UACAGGC 27	nucleic acid single linear
35 40 45	(B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:  (ii) SEQUENCE DESCRIPTION: SEQ ID  GUCUAACCAG AGAGACCCAG UACAGGC 27  (127) INFORMATION FOR SEQ ID NO: 126:	nucleic acid single linear

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(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 126:
     GUACUGGUC UCUCUGGUUA GACCA
                                          25
5
     (128) INFORMATION FOR SEQ ID NO:
                                         127:
               (i) SEQUENCE CHARACTERISTICS:
                       (A) LENGTH:
                                                    28
10
                       (B) TYPE:
                                                    nucleic acid
                       (C) STRANDEDNESS:
                                                    single
                       (D) TOPOLOGY:
                                                    linear
               (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 127:
15
     CACACAACAG ACGGGCACAC ACUACUUG
                                         28
     (129) INFORMATION FOR SEQ ID NO:
20
              (i) SEQUENCE CHARACTERISTICS:
                       (A) LENGTH:
                                                    25
                       (B) TYPE:
                                                    nucleic acid
                       (C) STRANDEDNESS:
25
                                                    single
                      (D) TOPOLOGY:
                                                    linear
              (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 128:
     CUGAGGAUC UCUAGUUACC AGAGU
                                              25
30
     (130) INFORMATION FOR SEQ ID NO:
                                          129:
              (i) SEQUENCE CHARACTERISTICS:
35
                      (A) LENGTH:
                                                   23
                      (B) TYPE:
                                                   nucleic acid
                      (C) STRANDEDNESS:
                                                   single
                      (D) TOPOLOGY:
                                                   linear
40
              (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 129:
    CUCUGGUAAC UAGAGAUCCC UCA
                                        23
     (131) INFORMATION FOR SEQ ID NO:
                                         130:
45
              (i) SEQUENCE CHARACTERISTICS:
                      (A) LENGTH:
                                                   23
                      (B) TYPE:
                                                   nucleic acid
50
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	(C) STRANDEDNESS: (D) TOPOLOGY:	single linear
5	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 130:
•	GUUCGGGCGC CACUGCUAGA GAU 23	
	(132) INFORMATION FOR SEQ ID NO: 131:	
10	(i) SEQUENCE CHARACTERISTICS:	
15	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	23 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 131:
20	GCAAGCCGAG UCCUGCGUCG AGA 23	
20	(133) INFORMATION FOR SEQ ID NO: 132:	
	(i) SEQUENCE CHARACTERISTICS:	
25	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	24 nucleic acid single linear
30	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 132:
	UGCGAGAGCG UCAGUAUUAA GCGG 24	•
	(134) INFORMATION FOR SEQ ID NO: 133:	
35	(i) SEQUENCE CHARACTERISTICS:	
40	<ul><li>(A) LENGTH:</li><li>(B) TYPE:</li><li>(C) STRANDEDNESS:</li><li>(D) TOPOLOGY:</li></ul>	36 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ	ID NO: 133:
45	CUACUUUGGA AUAUUGCUGG UGAUCCUUUC CAUCCC	36
	(135) INFORMATION FOR SEQ ID NO: 134:	
	(i) SEQUENCE CHARACTERISTICS:	
50		

5	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	33 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION: SEQ ID	NO: 134:
	CCAAUCCCC CUUUUCUUUU AAAAUUGUGG AUG	33
10	(136) INFORMATION FOR SEQ ID NO: 135:	
	(i) SEQUENCE CHARACTERISTICS:	
15	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	24: nucleic acid single linear
20	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 135:
	CUCGCCACUC CCCAGUCCCG CCCA 24	
	(137) INFORMATION FOR SEQ ID NO: 136:	
25	(i) SEQUENCE CHARACTERISTICS:	
30		24 nucleic acid single linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO:• 136:
35	CCGCUUAAUA CUGACGCUCU CGCA 24	
00	(138) INFORMATION FOR SEQ ID NO: 137:	
	(i) SEQUENCE CHARACTERISTICS:	
40	(A) LENGTH: (B) TYPE: (C) STRANDEDNESS: (D) TOPOLOGY:	36 nucleic acid single linear
45	(ii) SEQUENCE DESCRIPTION : SEQ ID	NO: 137:
	GGGAUGGAAA GGAUCACCAG CAAUAUUCCA AAGUAG	36
50	(139) INFORMATION FOR SEQ ID NO: 138:	

	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 33 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 138:
10	CAUCCACAAU UUUAAAAGAA AAGGGGGGAU UGG 33
	(140) INFORMATION FOR SEQ ID NO: 139:
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 24 (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
20	(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 139:
	UGGGCGGAC UGGGGAGUGG CGAG 24
25	
	Claims
30	1. An oligonucleotide consisting essentially of a sequence selected from the group of:
35	

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(SEQ ID NO: 1) GACTAGCGGAGGCTAGAAGGAGAGAGATGGG,
    (SEO ID NO: 2) GAAGGCTTTCAGCCCAGAAGTAATACCCATG,
    (SEQ ID NO: 3) ATTTGCATGGCTGCTTGATGTCCCCCCACT,
5
    (SEQ ID NO: 4) CTTCCCCTTGGTTCTCTCATCTGGCC,
    (SEO ID NO: 5) GTCATCCATCCTATTTGTTCCTGAAGGGTACTAGTAG,
    (SEQ ID NO: 6) CTCCCTGACATGCTGTCATCATTTCTTCTAGTG,
    (SEQ ID NO: 7) GTGGAAGCACATTGTACTGATATCTAATCCC,
10
    (SEQ ID NO: 8) GCTCCTCTATTTTGTTCTATGCTGCCCTATTTCTAA,
    (SEQ ID NO: 9) CCTTTGTGTGCTGGTACCCATGC,
    (SEQ ID NO:10) CTACTATTCTTTCCCCTGCACTGTACCCC,
15
    (SEQ ID NO:11) AAAGCCTTAGGCATCTCCTATGGCAGGAA,
    (SEQ ID NO:12) GCAGCTGCTTATATGCAGGATCTGAGGG,
    (SEQ ID NO:13) CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG,
20
    (SEQ ID NO:14) ATCTCTAGCAGTGGCGCCCGAACAGGGA,
    (SEQ ID NO:53) CCCATCTCTCTCTCTTCTAGCCTCCGCTAGTC,
    (SEQ ID NO:54) CATGGGTATTACTTCTGGGCTGAAAGCCTTC,
    (SEQ ID NO:55) AGTGGGGGGACATCAAGCAGCCATGCAAAT,
25
    (SEQ ID NO:56) GGCCAGATGAGAGAACCAAGGGGÄAG,
    (SEQ ID NO:57) CTACTAGTACCCTTCAGGAACAAATAGGATGGATGAC,
    (SEQ ID NO:58) CACTAGAAGAAATGATGACAGCATGTCAGGGAG,
30
    (SEO ID NO:59) GGGATTAGATATCAGTACAATGTGCTTCCAC,
    (SEQ ID NO:60) TTAGAAATAGGGCAGCATAGAACAAAAATAGAGGAGC,
    (SEQ ID NO:61) GCATGGGTACCAGCACAAAGG,
    (SEO ID NO: 62) GGGGTACAGTGCAGGGGAAAGAATAGTAG,
    (SEQ ID NO:63) TTCCTGCCATAGGAGATGCCTAAGGCTTT,
    (SEQ ID NO:64) CCCTCAGATCCTGCATATAAGCAGCTGC,
    (SEQ ID NO:65) CCCACTGCTTAAGCCTCAATAAAGCTTGCCTTG,
    (SEQ ID NO:66) TCCCTGTTCGGGCGCCACTGCTAGAGAT,
    (SEQ ID NO:67) GACUAGCGGAGGCUAGAAGGAGAGAGAUGGG,
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(SEQ ID NO:68) GAAGGCUUUCAGCCCAGAAGUAAUACCCAUG,
     (SEQ ID NO:69) AUUUGCAUGGCUGCUUGAUGUCCCCCACU,
     (SEQ ID NO:70) CUUCCCCUUGGUUCUCUCAUCUGGCC,
5
     (SEQ ID NO:71) GUCAUCCAUCCUAUUUGUUCCUGAAGGGUACUAGUAG,
     (SEQ ID NO:72) CUCCCUGACAUGCUGUCAUCAUUUCUUCUAGUG,
     (SEQ ID NO:73) GUGGAAGCACAUUGUACUGAUAUCUAAUCCC,
     (SEQ ID NO:74) GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA,
10
     (SEQ ID NO:75) CCUUUGUGUGCUGGUACCCAUGC,
     (SEQ ID NO:76) CUACUAUUCUUUCCCCUGCACUGUACCCC,
     (SEQ ID NO:77) AAAGCCUUAGGCAUCUCCUAUGGCAGGAA,
15
     (SEQ ID NO:78) GCAGCUGCUUAUAUGCAGGAUCUGAGGG,
     (SEQ ID NO:79) CAAGGCAAGCUUUAUUGAGGCUUAAGCAGUGGG,
     (SEQ ID NO:80) AUCUCUAGCAGUGGCGCCCGAACAGGGA,
20
     (SEQ ID NO:81) CCCAUCUCUCUCUUCUAGCCUCCGCUAGUC,
     (SEQ ID NO:82) CAUGGGUAUUACUUCUGGGCUGAAAGCCUUC,
     (SEQ ID NO:83) AGUGGGGGGACAUCAAGCAGCCAUGCAAAU,
     (SEQ ID NO:84) GGCCAGAUGAGAGAACCAAGGGGAAG,
25
     (SEQ ID NO:85) CUACUAGUACCCUUCAGGAACAAAUAGGAUGGAUGAC,
     (SEQ ID NO:86) CACUAGAAGAAAUGAUGACAGCAUGUCAGGGAG,
     (SEQ ID NO:87) GGGAUUAGAUAUCAGUACAAUGUGCUUCCAC,
30
     (SEQ ID NO:88) UUAGAAAUAGGGCAGCAUAGAACAAAAAUAGAGGAGO,
     (SEO ID NO:89) GCAUGGGUACCAGCACAAAGG,
     (SEQ ID NO:90) GGGGUACAGUGCAGGGGAAAGAAUAGUAG,
     (SEQ ID NO:91) UUCCUGCCAUAGGAGAUGCCUAAGGCUUU,
35
     (SEQ ID NO:92) CCCUCAGAUCCUGCAUAUAAGCAGCUGC,
     (SEQ ID NO:93) CCCACUGCUUAAGCCUCAAUAAAGCUUGCCUUG, and
      (SEQ ID NO:94) UCCCUGUUCGGGCGCCACUGCUAGAGAU.
40
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- 2. A nucleic acid hybrid formed between an oligonucleotide of claim 1 and a nucleotide polymer sufficiently complementary thereto to allow hybridization under stringent hybridization conditions.
- 45 3. A probe mix comprising an oligonucleotide of claim 1 and a helper probe.
  - 4. A probe mix as claimed in claim 3, wherein said helper probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 15) TGCGAGAGCGT-CAGTATTAAGCGG, complementary oligonucleotide sequence (SEQ ID NO: 95) CCGCTTAATACTGACGCTCTCGCA, and RNA equivalents thereto (SEQ ID NO: 132) UGCGAGAGCGU-CAGUAUUAAGCGG, and (SEQ ID NO: 136) CCGCUUAAUACUGACGCUCUCGCA; or

probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 16) CTACTTTGGAATATTGCTGGTGATCCTTTCCATCCC, the complementary oligonucleotide sequence (SEQ ID NO: 96) GGGATGGAAAGGATCACCAGCAATATTCCAAAGTAG, and RNA equivalents thereto (SEQ ID NO: 133)

CUACUUUGGAAUAUUGCUGGUGAUCCUUUCCAUCCC, and (SEQ ID NO: 137) GGGAUGGAAAGGAUCACCAGCAAUAUUCCAAAGUAG; or

50

said helper

probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 17) CCAATCCCCCCTTTTCTTTTAAAATTGTGGATG, the complementary oligonucleotide sequence (SEQ ID NO: 97) CATCCACAATTTTAAAAGAAAAGGGGGGGATTGG and RNA equivalents thereto (SEQ ID NO: 134) CCAAUCCCCCUUUUCUUUUAAAAUUGUGGAUG and (SEQ ID NO: 138) CAUCCACAAUUUUAAAAGAAAAGGGGGGGAUUGG; or

said helper

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probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 18) CTCGCCACTCCCAGTCCCGCCCA, the complementary oligonucleotide sequence (SEQ ID NO: 98)

TGGGCGGGACTGGGGAGTGGCGAG, and RNA equivalents thereto (SEQ ID NO: 135) CUCGCCA-CUCCCCAGUCCCGCCCA and (SEQ ID NO: 139) UGGGCGGGACUGGGGAGUGGCGAG.

- 5. An oligonucleotide consisting essentially of a sequence selected from the group of:
  - SEQ. ID. No. 5: GTCATCCATCCTATTTGTTCCTGAAGGGTACTAGTAG,
  - SEQ. ID. No. 10: CTACTATTCTTTCCCCTGCACTGTACCCC,
  - SEQ. ID. No. 71: GUCAUCCAUCCUAUUUGUUCCUGAAGGGUACUAGUAG, and
- SEQ. ID. No. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC.
  - 6. The oligonucleotide of claim 5, having a sequence of GTCATCCATCCTATTTGTTCCTGAAGGGTACTAG-TAG (SEQ. ID. NO. 5) or its RNA equivalent GUCAUCCAUCCUAUUUGUUCCUGAAGGGUACUAGUAG (SEQ. ID. NO. 71).
    - The oligonucleotide of claim 5, having a sequence of CTACTATTCTTTCCCCTGCACTGTACCCC (SEQ. ID. NO. 10) or its RNA equivalent CUACUAUUCUUUCCCCUGCACUGUACCCC (SEQ. ID. NO. 76).
- 8. An oligonucleotide consisting essentially of between 10 and 100 nucleotides, sufficiently complementary to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 1: 5'-GACTAGCGGAGGCTAGAAGGAGAGAGAGAGGGG-3' and SEQ. ID. No. 53: 5'-CCCATCTCTCTCTCTCTCGCTCGCTAGTC-3', and the RNA equivalents thereto, SEQ. ID. No. 67: 5'-GACUAGCGGAGGCUAGAAGGAGAGAGAGAGGGG-3' and SEQ. ID. No. 81: 5'-CCCAUCUCUCCCUU-CUAGCCUCCGCUAGUC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having nucleotide base sequence selected from a group consisting of SEQ. ID. No. 2: 5'-GAAGGCTTTCAGCCCAGAAGTAATACCCATG-3' and SEQ. ID. No. 54: 5'-CATGGGTAT-TACTTCTGGGCTGAAAGCCTTC-3', and the RNA equivalents thereto, SEQ. ID. No. 68: 5'-GAAGG-CUUUCAGCCCAGAAGUAAUACCCAUG-3' and SEQ. ID. No. 82: 5'-CAUGGGUAUUACUUCUGGGCU-GAAAGCCUUC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 3: 5'-ATTTGCATGGCTGCTTGATGTCCCCCCACT-3' and SEQ. ID. No. 55: 5'-AGTGGGGGGGACAT-CAAGCAGCCATGCAAAT-3', and the RNA equivalents thereto, SEQ. ID. No. 69: 5'-AUUUGCAUGG-CUGCUUGAUGUCCCCCCACU-3' and SEQ. ID. No. 83: 5'-AGUGGGGGGACAUCAAGCAGCCAUG-CAAAU-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 4: 5'-CTTCCCCTTGGTTCTCATCTGGCC-3', and SEQ. ID. No. 56: 5'-GGCCAGATGAGAGAAC-CAAGGGGAAG-3', and the RNA equivalents thereto, SEQ. ID. No. 70: 5'-CUUCCCCUUGGUUCUCU-CAUCUGGCC-3' and SEQ. ID. No 84: 5'-GGCCAGAUGAGAGAACCAAGGGGAAG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 5: 5'-GTCATCCATCCTATTTGTTCCTGAAGGGTACTAGTAG-3', and SEQ. ID. No. 57: 5'-CTACTAGTACCCTTCAGGAACAATAGGATGGATGAC-3', and the RNA equivalents thereto, SEQ. ID. No. 71: 5-

GUCAUCCAUCCUAUUUGUUCCUGAAGGGUACUAGUAG-3' and SEQ. ID. No. 85: 5'-CUACUA-GUACCCUUCAGGAACAAAUAGGAUGGAUGAC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

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to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 6: 5'-CTCCCTGACATGCTGTCATCATTTCTTCTAGTG-3', and SEQ. ID. No. 58: 5'-CACTAGAA-GAAATGATGACAGCATGTCAGGGAG-3', and the RNA equivalents thereto, SEQ. ID. No. 72: 5'-CUCCCUGACAUGCUGUCAUCAUUUCUUCUAGUG-3' and SEQ. ID. No. 86: 5'-CACUAGAAGAAAUGAUGA-CAGCAUGUCAGGGAG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 7: 5'-GTGGAAGCACATTGTACTGATATCTAATCCC-3', and SEQ. ID. No. 59: 5'-GGGATTAGATATCAGTACAATGTGCTTCCAC-3', and the RNA equivalents thereto, SEQ. ID. No. 73: 5'-GUGGAAGCACAUUGUACUGAUAUCUCAAUCCC-3' and SEQ. ID. No. 87: 5'-GGGAUUAGAUAUCAGUACAAUGUGCUUCCAC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 8: 5'-GCTCCTCTATTTTTGTTCTATGCTGCCCTATTTCTAA-3', and SEQ. ID. No. 60: 5'-TTAGAAA-TAGGGCAGCATAGAACAAAAATAGAGGAGC-3', and the RNA equivalents thereto, SEQ. ID. No. 74: 5'-GCUCCUCUAUUUUGUUCUAUGCUGCCCUAUUUCUAA-3' and SEQ. ID. No. 88: 5'-UUA-GAAAUAGGGCAGCAUAGAACAAAAAUAGAGGAGC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 9: 5'-CCTTTGTGTGCTGGTACCCATGC-3', and SEQ. ID. No. 61: 5'-GCATGGGTACCAGCACA-CAAAGG-3', and the RNA equivalents thereto, SEQ. ID. No. 75: 5'-CCUUUGUGUGCUGGUACC-CAUGC-3' and SEQ. ID. No. 89: 5'-GCAUGGGUACCAGCACACAAAGG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

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sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 10: 5,-CTACTATTCTTTCCCCTGCACTGTACCCC-3', and SEQ. ID. No. 62: 5'-GGGGTACAGTG-CAGGGGAAAGAATAGTAG-3', and the RNA equivalents thereto, SEQ. ID. No. 76: 5'-CUACUAUU-CUUUCCCUGCACUGUACCCC-3' and SEQ. ID. No. 90: 5'-GGGGUACAGUGCAGGGGAAAGAAUA-GUAG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 11: 5'-AAAGCCTTAGGCATCTCCTATGGCAGGAA-3', and SEQ. ID. No. 63: 5'-TTCCTGCCATAGGA-GATGCCTAAGGCTTT-3', and the RNA equivalents thereto, SEQ. ID. No. 77: 5'-AAAGCCUUAGGCAU-CUCCUAUGGCAGGAA-3' and SEQ. ID. No. 91: 5'-UUCCUGCCAUAGGAGAUGCCUAAGGCUUU-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 12: 5'-GCAGCTGCTTATATGCAGGATCTGAGGG-3', and SEQ. ID. No. 64: 5'-CCCTCAGATCCTG-CATATAAGCAGCTGC-3', and the RNA equivalents thereto, SEQ. ID. No. 78: 5'-GCAGCUGCUUAUAUGCAGGAUCUGAGGG-3' and SEQ. ID. No. 92: 5'-CCCUCAGAUCCUGCAUAUAAGCAGCUGC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCI at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 13: 5'-CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG-3', and SEQ. ID. No. 65: 5'-CCCACTGCT-TAAGCCTCAATAAAGCTTGCCTTG-3', and the RNA equivalents thereto, SEQ. ID. No. 79: 5'-CAAGG-CAAGCUUUAUUGAGGCUUAAGCAGUGGG-3' and SEQ. ID. No. 93: 5'-CCCACUGCUUAAGCCU-CAAUAAAGCUUGCCUUG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 14: 5'-ATCTCTAGCAGTGGCGCCCGAACAGGGA-3', and SEQ. ID. No. 66: 5'-TCCCTGTTCGGGCGCCCACTGCTAGAGAT-3', and the RNA equivalents thereto, SEQ. ID. No. 80: 5'-AU-

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    (X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),
    (X) CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),
    (X) GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),
10
    (X) GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),
    (X) CAGAAGGAGCCACCCCACAAGATTTA (SEQ. ID. NO. 23),
    (X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),
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    (X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),
    (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26),
    (X) CCATCCTATTTGTTCCTGAAGGGTAC (SEQ. ID. NO. 27),
    (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),
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(X) GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29),
     (X) TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),
     (X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),
5
     (X) GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),
     (X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33),
     (X) ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),
     (X) GCATTAGGAATCATTCAAGCACAACCAG (SEQ. ID. NO. 35),
10
     (X)GCACTGACTAATTTATCTACTTGTTCATTTCCTC (SEQ. ID. NO. 36),
     (X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO.
     37),
15
     (X) TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),
     (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),
     (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),
20
     (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41),
     (X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),
     (X) CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),
     (X) CAAGGGACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44),
25
     (X)GTCTAACCAGAGAGCCCAGTACAGGC (SEQ. ID. NO. 45),
     (X) GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),
     (X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
30
     (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
     (X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),
     (X)GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),
35
     (X)GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51),
     (X) CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99),
     (X) CUCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100),
     (X) GGCAAAUGGUACAUCAGGCCAUAUCACCUAG (SEQ. ID. NO. 101),
     (X) GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102),
     (X) CAGAAGGAGCCACCCCACAAGAUUUA (SEQ. ID. NO. 103),
     (X) GACCAUCAAUGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104),
45
     (X) CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105),
     (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106),
     (X) CCAUCCUAUUUGUUCCUGAAGGGUAC (SEQ. ID. NO. 107),
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(X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108),
      (X) GAAACCUUGUUGAGUCCAAAAUGCGAACCC (SEQ. ID. NO. 109),
      (X) UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110),
 5
      (X) CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111),
      (X) GUCAUGCUACUUUGGAAUAUUUCUGGUGAUCCUUU (SEQ. ID. NO. 112),
      (X) CAAUACAUGGAUGAUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113),
 10
      (X) ACCAAAGGAAUGGAGGUUCUUUCUGAUG (SEQ. ID. NO. 114),
      (X) GCAUUAGGAAUCAUUCAAGCACAACCAG (SEQ. ID. NO. 115),
      (X) GCACUGACUAAUUUAUCUACUUGUUCAUUUCCUC (SEQ. ID. NO. 116),
      (X) GGGAUUGGAGGAAAUGAACAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO.
15
      117),
      (X) UGUGUACAAUCUAGUUGCCAUAUUCCUGGACUACA (SEQ. ID. NO. 118),
      (X) CAAAUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119).
20
      (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120),
      (X) CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121),
      (X) GAGCCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122),
      (X) CUUCGUCGCUGUCUCCGCUUC (SEQ. ID. NO. 123),
25
      (X) CAAGGGACUUUCCGCUGGGGACUUUCC (SEQ. ID. NO. 124),
      (X) GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125),
      (X) GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126),
      (X) CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127),
      (X) CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128),
      (X) CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129),
35
      (X) GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and
      (X) GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131),
       where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or
       which enhances initiation or elongation by an RNA polymerase.
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    10. An oligonucleotide selected from the group of oligonucleotides consisting of:
        (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26)
45
      (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28)
      (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39)
      (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40)
50
      (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41)
      (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106)
      (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108)
      (X) CAAAUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119)
55
      (X)GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120) and
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(X) CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121),

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

11. A kit comprising two oligonucleotides selected from the group consisting of:

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5
     (X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),
     (X) CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),
     (X) GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),
10
     (X) GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),
     (X) CAGAAGGAGCCACCCCACAAGATTTA (SEQ. ID. NO. 23),
     (X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),
     (X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),
15
     (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26),
     (X) CCATCCTATTTGTTCCTGAAGGGTAC (SEQ. ID. NO. 27),
     (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),
20
     (X) GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29),
     (X) TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),
     (X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),
25
     (X) GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),
     (X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. 'ID. NO. 33),
     (X) ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),
     (X)GCATTAGGAATCATTCAAGCACAACCAG (SEQ. ID. NO. 35),
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     (X)GCACTGACTAATTTATCTACTTGTTCATTTCCTC (SEQ. ID. NO. 36),
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(X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO.
     37),
     (X) TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),
5
     (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),
     (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),
     (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41),
     (X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),
10
     (X) CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),
     (X) CAAGGGACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44),
     (X)GTCTAACCAGAGAGCCCAGTACAGGC (SEQ. ID. NO. 45),
15
     (X) GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),
     (X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
     (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
20
     (X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),
     (X)GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),
     (X)GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51),
     (X) CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99),
25
     (X) CUCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100),
     (X)GGCAAAUGGUACAUCAGGCCAUAUCACCUAG (SEQ. ID. NO. 101),
     (X) GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102),
30
     (X) CAGAAGGAGCCACCCCACAAGAUUUA (SEQ. ID. NO. 103),
     (X)GACCAUCAAUGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104),
     (X) CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105),
     (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106),
35
     (X) CCAUCCUAUUUGUUCCUGAAGGGUAC (SEQ. ID. NO. 107),
     (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108),
     (X) GAAACCUUGUUGAGUCCAAAAUGCGAACCC (SEQ. ID. NO. 109),
40
     (X) UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110),
     (X) CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111),
     (X) GUCAUGCUACUUUGGAAUAUUUCUGGUGAUCCUUU (SEQ. ID. NO. 112),
45
     (X) CAAUACAUGGAUGAUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113),
     (X) ACCAAAGGAAUGGAGGUUCUUUCUGAUG (SEQ. ID. NO. 114),
     (X)GCAUUAGGAAUCAUUCAAGCACAACCAG (SEQ. ID. NO. 115),
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- (X) GCACUGACUAAUUUAUCUACUUGUUCAUUUCCUC (SEQ. ID. NO. 116), (X) GGGAUUGGAGGAAAUGAACAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO. 5 117). (X) UGUGUACAAUCUAGUUGCCAUAUUCCUGGACUACA (SEQ. ID. NO. 118), (X) CAAAUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119), (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120), 10 (X) CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121), (X) GAGCCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122), (X) CUUCGUCGCUGUCUCCGCUUC (SEQ. ID. NO. 123), 15 (X) CAAGGGACUUUCCGCUGGGGACUUUCC (SEQ. ID. NO. 124), (X) GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125), (X) GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), (X) CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127), 20 (X) CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128), (X) CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129), (X) GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and
  - where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.
  - 12. A kit comprising two oligonucleotides selected from the group consisting of:

(X) GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131),

- (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26)
- (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28)
- (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39)
- (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40)
- (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41)
  - (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106)
  - (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108)
  - (X) CAAAUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119)
- 45 (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120) and
  - (X) CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121),
- where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.
  - 13. A kit comprising oligonucleotides having the following sequences: (X)CTCGACGCAG-GACTCGGCTTGCTG (SEQ. ID. NO. 19) or its RNA equivalent (X)CUCGACGCAGGACUCGGCUUG-CUG (SEQ. ID. NO. 99), and (X)CTCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20) or its RNA equivalent (X)CUCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100), and SEQ. ID. NO. 1: GACTAGCG-GAGGCTAGAAGGAGAGAGAGAGAGGGG or its RNA equivalent SEQ. ID. NO. 67: GACUAGCGGAGGCUA-GAAGGAGAGAGAGGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA

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polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences; (X)GGCAAATGGTACATCAGGCCA-TATCACCTAG (SEQ. ID. NO. 21) or its RNA equivalent (X)GGCAAAUGGUACAUCAGGCCAUAUCAC-CUAG (SEQ. ID. NO. 101), and (X)GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22) or its RNA equivalent (X)GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102), and SEQ. ID. NO. 2: GAAGGCTTTCAGCCCAGAAGTAATACCCATG or its RNA equivalent SEQ. ID. NO. 68: GAAGGCUUU-CAGCCCAGAAGUAAUACCCAUG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAGAAGGAGCCACCCCACAAGATTTA (SEQ. ID. NO. 23) or its RNA equivalent (X)CAGAAGGAGCCACCCCACAAGAUUUA (SEQ. ID. NO. 103), and (X)CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25) or its RNA equivalent (X)CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105), and SEQ. ID. NO. 3: ATTTG-CATGGCTGCTTGATGTCCCCCACT or its RNA equivalent SEQ. ID. NO. 69: AUUUGCAUGGCUGCUUGAUGUCCCCCCACU, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GACCATCAATGAGGAAGCTG-CAGAATG (SEQ. ID. NO. 24) or its RNA equivalent (X)GACCAUCAAUGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104), and (X)CCATCCTATTTGTTCCTGAAGGGTAC (SEQ. ID. NO. 27) or its RNA equivalent (X)CCAUCCUAUUUGUUCCUGAAGGGUAC (SEQ. ID. NO. 107), and SEQ. ID. NO. 4: CTTCCCCTTGGTTCTCTCATCTGGCC or its RNA equivalent SEQ. ID. NO. 70: CUUCCCCUUGGUUCU-CUCAUCUGGCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26) or its RNA equivalent (X)AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106), and (X)AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28) or its RNA equivalent (X)AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108), and SEQ. ID. NO. 5: GTCATCCATCCTATTTGTTCCTGAAGGGTACTAGTAG or its RNA equivalent SEQ. ID. NO. 71: GUCAUCCAUCCUAUUUGUUCCUGAAGGGUACUAGUAG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GAAACCTTGTTGAGTC-CAAAATGCGAACCC (SEQ. ID. NO. 29) or its RNA equivalent (X)GAAACCUUGUUGAGUCCAAAAUGC-GAACCC (SEQ. ID. NO. 109), and (X)TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30) or its RNA equivalent (X)UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110), and SEQ. ID. NO. 6: CTCCCTGACATGCTGTCAT-CATTCTTCTAGTG or its RNA equivalent SEQ. ID. NO. 72: CUCCCUGACAUGCUGUCAUCAUUUCUU-CUAGUG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAGTACTGGATGTGGGT-GATGC (SEQ. ID. NO. 31) or its RNA equivalent (X)CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111), and (X)GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO: 32) or its RNA equivalent (X)GUCAUGCUACUUUGGAAUAUUUCUGGUGAUCCUUU (SEQ. ID. NO. 112), and SEQ. ID. NO. 7: GTGGAAGCACATTGTACTGATATCTAATCCC or its RNA equivalent SEQ. ID. NO. 73: GUGGAAGCACAUUGUACUGAUAUCUAAUCCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation. by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33) or its RNA equivalent (X)CAAUACAUGGAUGAUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113), and (X)ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34) or its RNA equivalent (X)ACCAAAGGAAUGGAGGUUCUUUCUGAUG (SEQ. ID. NO. 114), and SEQ. ID. NO. 8: GCTCCTCTATTTTTGTTCTATGCTGCCCTATTTCTAA or its RNA equivalent SEQ. ID. NO. 74: GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GCATTAGGAATCATTCAAGCA-CAACCAG (SEQ. ID. NO. 35) or its RNA equivalent (X)GCAUUAGGAAUCAUUCAAGCACAACCAG (SEQ. ID. NO. 115), and (X)GCACTGACTAATTTATCTACTTGTTCATTTCCTC (SEQ. ID. NO. 36) or its RNA equivalent (X)GCACUGACUAAUUUAUCUACUUGUUCAUUUCCUC (SEQ. ID. NO. 116), and SEQ. ID. NO. 9: CCTTTGTGTGCTGGTACCCATGC or its RNA equivalent SEQ. ID. NO. 75: CCUUUGUGUG-CUGGUACCCAUGC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

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comprising oligonucleotides having the following sequences: (X)GGGATTGGAGGAAATGAA-CAAGTAGATAAATTAGTCAG (SEQ. ID. NO. 37) or its RNA equivalent (X)GGGAUUGGAGGAAAUGAA-CAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO. 117), and (X)TGTGTACAATCTAGTTGCCATATTCCTG-GACTACA (SEQ. ID. NO. 38) or its RNA equivalent (X)UGUGUACAAUCUAGUUGCCAUAUUCCUGGA-CUACA (SEQ. ID. NO. 118), where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39) or its RNA equivalent (X)CAAAUGGCAGUAUUCAUCACA (SEQ. ID. NO. 119), and (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40) or its RNA equivalent (X)GUUUGUAUGUCU-GUUGCUAUUAU (SEQ. ID. NO. 120), and SEQ. ID. NO. 10: CTACTATTCTTTCCCCTGCACTGTACCCC or its RNA equivalent SEQ. ID. NO. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAAATGGCAGTATTCATCCACA (SEQ. ID. NO, 39) or its RNA equivalent (X)CAAAUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119), and (X)CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41) or its RNA equivalent (X)CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121), and SEQ. ID. NO. 10: CTACTATTCTTTCCCCTGCACTGTACCCC or its RNA equivalent SEQ. ID. NO. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase: or

comprising oligonucleotides having the following sequences: (X)GAGCCCTGGAAGCATCCAG-GAAGTCAG (SEQ. ID. NO. 42) or its RNA equivalent (X)GAGCCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122), and (X)CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43) or its RNA equivalent (X)CUUCGUCGCUGUCCGCUUC (SEQ. ID. NO. 123), and SEQ. ID. NO. 11: AAAGCCTTAGG-CATCTCCTATGGCAGGAA or its RNA equivalent SEQ. ID. NO. 77: AAAGCCUUAGGCAUCUCCUAUGG-CAGGAA, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAAGGGACTTTCCGCTGGG-GACTTTCC (SEQ. ID. NO. 44) or its RNA equivalent (X)CAAGGGACUUUCCGCUGGGGACUUUCC (SEQ. ID. NO. 124), and (X)GTCTAACCAGAGAGCCCAGTACAGGC (SEQ. ID. NO. 45) or its RNA equivalent (X)GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125), and SEQ. ID. NO. 12: GCAGCTGCTTATATGCAGGATCTGAGGG or its RNA equivalent SEQ. ID. NO. 78: GCAGCUGCUUAUAUGCAGGAUCUGAGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

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comprising oligonucleotides having the following sequences: (X)GTACTGGGTCTCTCTGGTTA-GACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), and (X)CACACACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47) or its RNA equivalent (X)CACACACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127), and SEQ. ID. NO. 13: CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAGCUUAUUGAGGCUUAAGCAGUGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GTACTGGGTCTCTCTGGTTA-GACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), and (X)CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48) or its RNA equivalent (X)CU-GAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128), and SEQ. ID. NO. 13: CAAGGCAAGCTTTATT-GAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAGCUUUAUUGAGG-CUUAAGCAGUGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GTACTGGGTCTCTCTGGTTA-GACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), and (X)GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50) or its RNA equivalent (X)GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and SEQ. ID. NO. 13: CAAGGCAAGCTT-TATTGAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAGCUUUAUU-GAGGCUUAAGCAGUGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CTCTGGTAACTAGAGATCCCT-CA (SEQ. ID. NO. 49) or its RNA equivalent (X)CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129), and (X)GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51) or its RNA equivalent (X)GCAAGCCGA-

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GUCCUGCGUCGAGA (SEQ. ID. NO. 131), and SEQ. ID. NO. 14: ATCTCTAGCAGTGGCGCCCGAA-CAGGGA or its RNA equivalent SEQ. ID. NO. 80: AUCUCUAGCAGUGGCGCCCGAACAGGGA, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

- 14. A method for selectively amplifying Human Immunodeficiency Virus type 1 nucleic acid in a sample, comprising the step of amplifying said nucleic acid with one or more oligonucleotides selected from the group consisting of:
- (X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),
  - (X) CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),
  - (X) GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),
- (X) GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),
  - (X) CAGAAGGAGCCACCCCACAAGATTTA (SEQ. ID. NO. 23),
  - (X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),
  - (X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),
  - (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26),
  - (X) CCATCCTATTTGTTCCTGAAGGGTAC (SEQ. ID. NO. 27),
  - (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),
- 25 (X) GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29),
  - (X)TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),
  - (X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),
  - (X)GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),
    - (X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33),
    - (X) ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),
    - (X)GCATTAGGAATCATTCAAGCACAACCAG (SEQ. ID. NO. 35),
    - (X)GCACTGACTAATTTATCTACTTGTTCATTTCCTC (SEQ. ID. NO. 36),
    - (X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO. 37),
- 40 (X)TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),
  - (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),
  - (X) GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),
- (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41),

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(X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),
    (X) CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),
    (X) CAAGGGACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44),
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    (X)GTCTAACCAGAGAGCCCAGTACAGGC (SEQ. ID. NO. 45),
    (X) GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),
    (X) CACACAACAGACGGCACACACTACTTG (SEQ. ID. NO. 47),
    (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
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    (X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),
    (X)GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),
    (X)GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51)
    (X) CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99),
    (X) CUCCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100),
    (X) GGCAAAUGGUACAUCAGGCCAUAUCACCUAG (SEQ. ID. NO. 101),
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    (X) GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102),
    (X) CAGAAGGAGCCACCCCACAAGAUUUA (SEQ. ID. NO. 103),
    (X)GACCAUCAAUGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104),
    (X) CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105),
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    (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106),
    (X) CCAUCCUAUUUGUUCCUGAAGGGUAC (SEQ. ID. NO. 107),
    (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108),
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    (X) GAAACCUUGUUGAGUCCAAAAUGCGAACCC (SEQ. ID. NO. 109),
    (X) UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110),
    (X) CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111),
    (X)GUCAUGCUACUUUGGAAUAUUUCUGGUGAUCCUUU (SEQ. ID. NO. 112),
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    (X) CAAUACAUGGAUGAUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113),
    (X) ACCAAAGGAAUGGAGGUUCUUUCUGAUG (SEQ. ID. NO. 114),
    (X)GCAUUAGGAAUCAUUCAAGCACAACCAG (SEQ. ID. NO. 115),
40
    (X)GCACUGACUAAUUUAUCUACUUGUUCAUUUCCUC (SEQ. ID. NO. 116),
    (X) GGGAUUGGAGGAAAUGAACAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO.
     117),
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     (X) UGUGUACAAUCUAGUUGCCAUAUUCCUGGACUACA (SEQ. ID. NO. 118),
     (X) CAAAUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119),
     (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120),
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- (X) CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121), (X) GAGCCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122), (X) CUUCGUCGCUGUCUCCGCUUC (SEQ. ID. NO. 123), 5 (X) CAAGGGACUUUCCGCUGGGGACUUUCC (SEQ. ID. NO. 124), (X) GUCUAACCAGAGAGCCCAGUACAGGC (SEQ. ID. NO. 125), (X) GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), 10 (X) CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127), (X) CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128), (X) CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129), (X) GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and 15 (X)GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131) where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase. 20
  - 15. A method for selectively amplifying Human Immunodeficiency Virus type 1 nucleic acid in a sample, comprising the step of amplifying said nucleic acid with one or more oligonucleotides selected from the group consisting of:
    - (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26)
    - (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28)
    - (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39)
    - (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40)
    - (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41)
    - (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106)
  - (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108)
    - (X) CAAAUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119)
    - (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120) and
    - (X) CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121),

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

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16. A method for detecting Human Immunodeficiency Virus type 1 nucleic acid in a sample comprising the step of hybridizing nucleic acid obtained directly or amplified from said sample with an oligonucleotide selected from the group consisting of:

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(SEO ID NO: 1) GACTAGCGGAGGCTAGAAGGAGAGAGATGGG,
    (SEQ ID NO: 2) GAAGGCTTTCAGCCCAGAAGTAATACCCATG,
    (SEQ ID NO: 3) ATTTGCATGGCTGCTTGATGTCCCCCCACT,
    (SEQ ID NO: 4) CTTCCCCTTGGTTCTCTCATCTGGCC,
    (SEQ ID NO: 5) GTCATCCATCCTATTTGTTCCTGAAGGGTACTAGTAG,
    (SEQ ID NO: 6) CTCCCTGACATGCTGTCATCATTTCTTCTAGTG,
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    (SEQ ID NO: 7) GTGGAAGCACATTGTACTGATATCTAATCCC,
    (SEQ ID NO: 8) GCTCCTCTATTTTTGTTCTATGCTGCCCTATTTCTAA,
    (SEQ ID NO: 9) CCTTTGTGTGCTGGTACCCATGC,
    (SEQ ID NO:10) CTACTATTCTTTCCCCTGCACTGTACCCC,
    (SEQ ID NO:11) AAAGCCTTAGGCATCTCCTATGGCAGGAA,
    (SEO ID NO:12) GCAGCTGCTTATATGCAGGATCTGAGGG,
    (SEQ ID NO:13) CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG,
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    (SEO ID NO:14) ATCTCTAGCAGTGGCGCCCGAACAGGGA,
    (SEQ ID NO:53) CCCATCTCTCTCTCTAGCCTCCGCTAGTC,
    (SEQ ID NO:54) CATGGGTATTACTTCTGGGCTGAAAGCCTTC,
    (SEQ ID NO:55) AGTGGGGGGACATCAAGCAGCCATGCAAAT,
    (SEQ ID NO:56) GGCCAGATGAGAGAACCAAGGGGAAG,
    (SEQ ID NO:57) CTACTAGTACCCTTCAGGAACAAATAGGATGATGAC,
    (SEQ ID NO:58) CACTAGAAGAAATGATGACAGCATGTCAGGGAG,
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    (SEQ ID NO:59) GGGATTAGATATCAGTACAATGTGCTTCCAC,
    (SEQ ID NO:60) TTAGAAATAGGGCAGCATAGAACAAAAATAGAGGAGC,
    (SEO ID NO:61) GCATGGGTACCAGCACAAAGG,
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(SEQ ID NO:62) GGGGTACAGTGCAGGGGAAAGAATAGTAG,
       (SEQ ID NO:63) TTCCTGCCATAGGAGATGCCTAAGGCTTT,
       (SEQ ID NO:64) CCCTCAGATCCTGCATATAAGCAGCTGC,
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       (SEQ ID NO:65) CCCACTGCTTAAGCCTCAATAAAGCTTGCCTTG,
       (SEQ ID NO:66) TCCCTGTTCGGGCGCCACTGCTAGAGAT,
       (SEQ ID NO:67) GACUAGCGGAGGCUAGAAGGAGAGAUGGG,
       (SEQ ID NO:68) GAAGGCUUUCAGCCCAGAAGUAAUACCCAUG,
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       (SEQ ID NO:69) AUUUGCAUGGCUGCUUGAUGUCCCCCCACU,
       (SEQ ID NO:70) CUUCCCCUUGGUUCUCUCAUCUGGCC,
       (SEQ ID NO:71) GUCAUCCAUCCUAUUUGUUCCUGAAGGGUACUAGUAG,
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       (SEQ ID NO:72) CUCCCUGACAUGCUGUCAUCAUUUCUUCUAGUG,
       (SEQ ID NO:73) GUGGAAGCACAUUGUACUGAUAUCUAAUCCC,
       (SEQ ID NO:74) GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA,
20
       (SEQ ID NO:75) CCUUUGUGUGCUGGUACCCAUGC,
       (SEQ ID NO:76) CUACUAUUCUUUCCCCUGCACUGUACCCC,
       (SEQ ID NO:77) AAAGCCUUAGGCAUCUCCUAUGGCAGGAA,
       (SEQ ID NO:78) GCAGCUGCUUAUAUGCAGGAUCUGAGGG,
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       (SEQ ID NO:79) CAAGGCAAGCUUUAUUGAGGCUUAAGCAGUGGG,
       (SEQ ID NO:80) AUCUCUAGCAGUGGCGCCCGAACAGGGA,
       (SEQ ID NO:81) CCCAUCUCUCUCUUCUAGCCUCCGCUAGUC,
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       (SEQ ID NO:82) CAUGGGUAUUACUUCUGGGCUGAAAGCCUUC,
       (SEQ ID NO:83) AGUGGGGGGACAUCAAGCAGCCAUGCAAAU,
       (SEO ID NO:84) GGCCAGAUGAGAGAACCAAGGGGAAG,
       (SEQ ID NO: 35) CUACUAGUACCCUUCAGGAACAAUAGGAUGGAUGAC,
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       (SEQ ID NO:86) CACUAGAAGAAAUGAUGACAGCAUGUCAGGGAG,
       (SEQ ID NO:87) GGGAUUAGAUAUCAGUACAAUGUGCUUCCAC,
       (SEQ ID NO:88) UUAGAAAUAGGGCAGCAUAGAACAAAAAUAGAGGAGC,
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       (SEO ID NO:89) GCAUGGGUACCAGCACAAAGG,
       (SEQ ID NO:90) GGGGUACAGUGCAGGGGAAAGAAUAGUAG,
       (SEQ ID NO:91) UUCCUGCCAUAGGAGAUGCCUAAGGCUUU,
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       (SEQ ID NO:92) CCCUCAGAUCCUGCAUAUAAGCAGCUGC,
       (SEO ID NO:93) CCCACUGCUUAAGCCUCAAUAAAGCUUGCCUUG, and
        (SEQ ID NO:94) UCCCUGUUCGGGCGCCACUGCUAGAGAU.
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17. A method for detecting Human Immunodeficiency Virus type 1 nucleic acid in a sample comprising the step of hybridizing nucleic acid obtained directly or amplified from said sample with an oligonucleotide selected from the group consisting of:

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- SEQ. ID. NO. 5: GTCATCCATCCTATTTGTTCCTGAAGGGTACTAGTAG,
- SEQ. ID. NO. 10: CTACTATTCTTTCCCCTGCACTGTACCCC,
- SEQ. ID. NO. 71: GUCAUCCAUCCUAUUUGUUCCUGAAGGGUACUAGUAG, and
- SEQ. ID. NO. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC.
- 18. A method for detecting Human Immunodeficiency Virus type 1 nucleic acid comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19) or its RNA equivalent (X)CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99), and (X)CTCCCCGGCTTAATACTGACGCT (SEQ. ID. NO. 20) or its RNA equivalent (X)CUCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 1: GACTAGCGGAGGCTAGAAGGAGAGAGAGAGAGAGGG or its RNA equivalent ID. NO. 67: GACUAGCGGAGGCUAGAAGGAGAGAGAGAGGG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21) or its RNA equivalent (X)GGCAAAUGGUACAUCAGGCCAUAUCACCUAG (SEQ. ID. NO. 101), and (X)GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22) or its RNA equivalent (X)GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 2: GAAGGCTTTCAGCCCAGAAGTAATACCCATG or its RNA equivalent SEQ. ID. NO. 68: GAAGGCUUUCAGCCCAGAAGUAAUACCCAUG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAGAAG-GAGCCACCCACAGATTTA (SEQ. ID. NO. 23) or its RNA equivalent (X)CAGAAGAGCCACCCA-CAAGAUUUA (SEQ. ID. NO. 103), and (X)CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25) or its RNA equivalent (X)CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 3: ATTTG-CATGGCTGCTTGATGTCCCCCCACT or its RNA equivalent SEQ. ID. NO. 69: AUUUGCAUGGCUGCUUGAUGUCCCCCCACU; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

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comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GACCAT-CAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24) or its RNA equivalent (X)GACCAUCAAUGAGGAAG-CUGCAGAAUG (SEQ. ID. NO. 104), and (X)CCATCCTATTTGTTCCTGAAGGGTAC (SEQ. ID. NO. 27) or its RNA equivalent (X)CCAUCCUAUUUGUUCCUGAAGGGUAC (SEQ. ID. NO. 107), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 4: CTTCCCCTTGGTTCTCATCTGGCC or its RNA equivalent SEQ. ID. NO. 70: CUUCCCCUUGGUUCU-CUCAUCUGGCC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)AGTGA-CATAGCAGGAACTA (SEQ. ID. NO. 26) or its RNA equivalent (X)AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106), and (X)AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28) or its RNA equivalent (X)AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 5: GTCATCCATCCTATTTGTTCCT-GAAGGGTACTAGTAG or its RNA equivalent SEQ. ID. NO. 71: GUCAUCCAUCCUAUUUGUUCCU-GAAGGGUACUAGUAG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29) or its RNA equivalent (X) GAAACCUUGUUGAGUCCAAAAUGCCAACCC (SEQ. ID. NO. 109), and (X)TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30) or its RNA equivalent (X)UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 6: CTCCCTGACATGCTGTCATCATTTCTTCTAGTG or its RNA equivalent SEQ. ID. NO. 72: CUCCCUGACAUGCUGUCAUCAUUUCUUCUAGUG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

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comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAG-TACTGGATGTGGGTGATGC (SEQ. ID. NO. 31) or its RNA equivalent (X)CAGUACUGGAUGUGGGU-GAUGC (SEQ. ID. NO. 111), and (X)GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32) or its RNA equivalent (X)GUCAUGCUACUUUGGAAUAUUUCUGGUGAUCCUUU (SEQ. ID. NO. 112), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 7: GTGGAAGCACATTGTACTGATATCTAATCCC or its RNA equivalent SEQ. ID. NO. 73: GUGGAAGCACAUUGUACUGAUAUCUAAUCCC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAATA-CATGATGATGTATGTAGGATCTGAC (SEQ. ID. NO. 33) or its RNA equivalent (X)CAAUACAUG-GAUGAUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113), and (X) ACCAAAGGAATG-GAGGTTCTTTCTGATG (SEQ. ID. NO. 34) or its RNA equivalent (X)ACCAAAGGAAUGGAGGUUCUUU-CUGAUG (SEQ. ID. NO. 114), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 8: GCTCCTCTATTTTTGTTCTATGCTGCCCTATTTCTAA or its RNA equivalent SEQ. ID. NO. 74: GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GCAT-TAGGAATCATTCAAGCACAACCAG (SEQ. ID. NO. 35) or its RNA equivalent (X)GCAUUAGGAAU-CAUUCAAGCACAACCAG (SEQ. ID. NO. 115), and (X)GCACTGACTAATTTATCTACTTGTT-CATTTCCTC (SEQ. ID. NO. 36) or its RNA equivalent (X)GCACUGACUAAUUUAUCUACUUGUU-CAUUUCCUC (SEQ. ID. NO. 116), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 9: CCTTTGTGTGCTGGTACCCATGC or its RNA equivalent SEQ. ID. NO. 75: CCUUUGUGUGCUGGUACCCAUGC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39) or its RNA equivalent (X)CAAAUGGCAGUAUU-CAUCCACA (SEQ. ID. NO. 119), and (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40) or its RNA equivalent (X)GUUUGUAUGUUUGCUAUUAU (SEQ. ID. NO. 120), or (X)CCCTTCACCTTTCCA-GAG (SEQ. ID. NO. 41) or its RNA equivalent (X)CCCUUCACCUUUCCAGAG (SEQ. ID. NO. 121), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 10: CTACTATTCTTTCCCTGCACTGTACCCC or its RNA equivalent SEQ. ID. NO. 76: CUACUAUU-CUUUCCCCUGCACUGUACCCC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42) or its RNA equivalent (X)GAGCCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122), and (X)CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43) or its RNA equivalent (X)CUUCGUCGCUGUCUCCGCUUC (SEQ. ID. NO. 123), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 11: AAAGCCTTAGGCATCTCCTATGGCAGGAA or its RNA equivalent SEQ. ID. NO. 77: AAAGCCUUAGGCAUCUCCUUAUGGCAGGAA; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAAGG-GACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44) or its RNA equivalent (X)CAAGGGACUUUCCG-CUGGGGACUUUCC (SEQ. ID. NO. 124), and (X)GTCTAACCAGAGAGACCCAGTACAGGC (SEQ. ID. NO. 45) or its RNA equivalent (X)GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125), and detecting the amplified nucleic acid with an oligonucleotide comprising the SEQ. ID. NO. 12: GCAGCTGCT-TATATGCAGGATCTGAGGG or its RNA equivalent SEQ. ID. NO. 78: GCAGCUGCUUAUAUGCAGGAU-CUGAGGG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO. 37) or its RNA equivalent (X)GGGAUUGGAGGAAAUGAACAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO. 117), and (X)TGTGTA-CAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38) or its RNA equivalent (X)UGUGUACAAU-CUAGUUGCCAUAUUCCUGGACUACA (SEQ. ID. NO. 118), and detecting the amplified nucleic acid with an oligonucleotide; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers

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(X)GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCU-CUCUGGUUAGACCA (SEQ. ID. NO. 126), and either

- (X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
- (X) CACACAACAGACGGCACACACUACUUG (SEQ. ID. NO. 127),
- (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
- (X) CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128),
- (X)GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50) or
- (X) GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130),

and detecting the amplified nucleic acid with an oligonucleotide comprising the SEQ. ID. NO. 13: CAAGG-CAAGCTTTATTGAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAG-CUUUAUUGAGGCUUAAGCAGUGGG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49) or its RNA equivalent (X)CUCUGGUAACUAGA-GAUCCCUCA (SEQ. ID. NO. 129), and (X)GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51) or its RNA equivalent (X)GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 14: ATCTCTAG-CAGTGGCGCCCGAACAGGGA or its RNA equivalent SEQ. ID. NO. 80: AUCUCUAGCAGUGGCGCCCGAACAGGGA; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

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11) Publication number: 0 617 132 A3

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## **EUROPEAN PATENT APPLICATION**

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- (54) Probes and method to detect human immunodeficiency virus type 1.
- (57) Amplification oligonucleotides and hybridization assay probes are provided which distinguish Human Immunodeficiency Virus type 1 from other viruses found in human blood tissues.

The probes are nucleotide polymers which hybridize to the nucleic acid region of Human Immunodeficiency Virus type 1 corresponding to bases 763-793 of HIV type 1, (HXB2 isolate GenBank accession number KO3455), or any of the regions corresponding to bases 1271-1301, 1358-1387, 1464-1489, 1501-1540, 1813-1845, 2969-2999, 3125-3161, 4148-4170,4804-4832, 5950-5978, 9496-9523, 510-542 and 624-651.

FP 0 617 132 AS



# **EUROPEAN SEARCH REPORT**

Application Number EP 94 30 2196

Category	Citation of document with of relevant pa	indication, where appropriate,	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
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	* the whole documer	nt *	15,15,16	
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·	Place of search	Date of completion of the search		Cominer
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X : pari Y : pari doc	CATEGORY OF CITED DOCUME icularly relevant if taken alone icularly relevant if combined with an iment of the same category inological background -written disclosure	E : eurlier patent doc after the filing di other D : document cited i L : document cited fo	nument, but publication or other reasons	invention shed on, or



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Y:pa do A:tec O:no	CATEGORY OF CITED DOCUME rticularly relevant if taken alone rticularly relevant if combined with an cument of the same category theological background o-written disclosure emmediate document	E: earlier patent do after the filing d other D: document cited L: document cited	cument, but plate in the application other reason	published on, or tion



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European Patent

Office

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C	CLAIMS INCURRING FEES					
_	The state of the s					
The present European patent application comprised at the time of filing more than ten claims.						
_	All claims lees have been paid within the prescribed time limit. The present European search report has been					
	drawn up for all claims					
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	Only part of the claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid,					
	report has been drawn up for the matter dams and for those dams to mind dams been drawn up for the matter dams and for the second secon					
	namety claims:					
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	ACK OF UNITY OF INVENTION					
The Sear	rch Division considers that the present European patent application does not comply with the requirement of unity of					
invention	and relates to several inventions or groups of inventions,					
namely:						
	Claims 1-8,13 partly,16,17,18 partly: Oligonucleotides					
1 .	for the detection of human immunodefiency virus					
	type I and their use.					
	and an area and as as partly. Oligopucleotides					
2.	Claims 9-12,13 partly,14,15,18 partly: Oligonucleotides for the amplification of human immunodeficiency					
	virus type I and their use.					
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X	All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.					
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П	Only part of the further search fees have been paid within the fixed time limit. The present European search					
	report has been drawn up for those parts of the European patent application which relate to the inventions in					
	respects of which search fees have been paid.					
	namely claims:					
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	None of the further search fees has been paid within the fixed time limit. The present European search report					
	has been drawn up for those parts of the European patent application which relate to the invention first					
	mentioned in the claims,					
	namely claims.					

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